PREVALENCE, ASSOCIATED FACTORS OF NICOTINE DEPENDENCE AND DISEASE SEVERITY IN PATIENTS WITH SCHIZOPHRENIA

By

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Dissertation Submitted in Partial Fulfillment of the Requirement for the Degree of Masters in Psychological Medicine

DEPARTMENT OF PSYCHOLOGICAL MEDICINE

FACULTY OF MEDICINE

UNIVERSITY OF MALAYA

KUALA LUMPUR

2012

UNIVERSITI MALAYA

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Name of Degree: MASTERS OF PSYCHOLOGICAL MEDICINE

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ACKNOWLEDGEMENT

In the name of Allah, the Most Gracious, the Most Merciful.

Above all, I thank God for all His blessings.

My deepest and most sincere gratitude and appreciation to my supervisors, Associate Professor Dr Stephen Jambunathan and Dr R. Parameswaran for their invaluable support, encouragement, suggestion and guidance from the initation until completion of this research.

A heartfelt note of thanks goes to Dr Ng Chong Guan, lecturer in the Department of Psychological Medicine in University of Malaya for his invaluable advise and guidance in the statistical analyses of this study.

I would also like to thank the staff in the Department of Psychiatry and Mental Health, Hospital Tuanku Ja'afar, Seremban and colleagues who have, either directly or indirectly, involved in the evolution of this research.

A special note of thanks goes to all the patients who were willing participants in this study.

This study would not have come to fruition without the love and undying support and understanding from my beloved husband, Dr Abdul Fattah bin Abdul Wahab. To our children, Muhammad Irham, Nur Ilyana Nasrin, Muhammad Irfan and Muhammad Ikhwan, although it was not an easy journey, I thank God that you were all there beside me all the way.

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LIST OF ABBREVIATIONS

BPRS	: Brief Psychiatric Rating Scale
CI	: confidence interval
CIDI	: Composite International Diagnostic Interview
DALY	: disability-adjusted life years
DSM	: Diagnostic and Statistical Manual
ECA	: Epidemiologic Catchment Area
FTND	: Fagerstrom Test for Nicotine Dependence
FTQ	: Fagerstrom Tolerance Questionnaire
GABA	: γ-aminobutyric acid
HIS	: Heavy Smoking Index
HTJS	: Hospital Tuanku Ja'afar, Seremban
ICD	: International Classification of Disease
M.I.N.I.	: Mini International Neuropsychiatric Interview
nAchR	: nicotine acetylcholine receptor
OR	: odds ratio
PANSS	: Positive and Negative Syndrome Scale
SCAN	: Schedules for Clinical Assessment in Neuropsychiatry
SCID	: Structured Clinical Interview for DSM-IV Disorders
SD	: standard deviation
SE	: standard error

SMR	: standardized mortality ratio
SPSS	: Statistical Package for Social Studies
SUD	: substance used disorder
WHO	: World Health Organisation
YLD	: years lived with disability

ABSTRAK

Pengenalan: Kajian telah menunjukkan secara konsisten bahawa pesakit dengan skizofrenia merokok pada kadar yang lebih tinggi dibandingkan dengan populasi umum. Kebergantungan nikotin, jenis kebergantungan substans paling kerap di kalangan pesakit skizofrenia, akan meningkatkan morbidity dan mortality kumpulan pesakit ini. Sehingga kini, tiada data tempatan berkaitan merokok dan kebergantungan nikotin di kalangan pesakit skizofrenia dapat diperolehi.

Objektif: Kajian ini bertujuan untuk menentukan prevalens merokok dan kebergantungan nikotin di kalangan sebuah sampel pesakit luar dengan diagnosis skizofrenia, factor-faktor yang berkaitan dengannya dan keterukan penyakit di dalam sampel ini.

Metodologi: Ini merupakan sebuah kajian keratan rentas seramai 181 orang pesakit dengan diagnosa skizofrenia di sebuah klinik pesakit luar psikiatrik sebuah hospital negeri. Diagnosa pesakit telah dipastikan menggunakan M.I.N.I. Pesakit yang memenuhi kriteria kajian kemudiannya dinilai tahap keterukan penyakit menggunakan PANSS. Pesakit yang merokok diminta untuk memenuhkan FTND. Kesemua peserta kajian kemudian diuji tahap karbon monoksida dalam udara yang dihembus menggunakan sebuah alat yang boleh dipegang di tangan.

Keputusan: Prevalens perokok di dalam sampel kajian adalah 38.1% dan 73.9% daripada mereka bergantung kepada nikotin. Perokok dikaitkan dengan jantina lelaki (OR 62.36, $p<0.01$), Melayu (OR 3.03, $p<0.05$), pendapatan bulanan lebih daripada RM500 (OR 0.43, $p<0.01$) dan menggunakan dadah ataupun alcohol (OR 12.96, $p<0.01$). Walau

bagaimanapun, faktor-faktor yang sama tiada kaitan dengan kebergantungan nikotin. Tiada kaitan didapati di antara skor FTND dan skor PANSS.

Kesimpulan: Prevalens merokok dan kebergantungan nikotin adalah amat signifikan. Ia dapat dikaitkan dengan pendapatan bulanan yang lebih tinggi. Perkhidmatan yang khusus adalah wajar untuk menangani isu ini. Di masa hadapan, kajian tempatan yang dijalankan dalam bidang ini amatlah perlu bagi mengenalpasti fakto-faktor lain yang berkaitan dengannya.

ABSTRACT

Introduction: Studies have consistently shown that people with schizophrenia smoke at higher rates than the general population. Nicotine dependence, the commonest substance use disorder in patients with schizophrenia would increase the morbidity and mortality in this group of patients. To date, there have been no local data pertaining to smoking and nicotine dependence in patients with schizophrenia.

Objective: This study aimed to determine the prevalence of smoking and nicotine dependence in a sample of outpatients with schizophrenia, factors associated with it and the severity of disease in the study sample.

Methods: This was a cross-sectional study of 181 patients with a diagnosis of schizophrenia in the outpatient psychiatric clinic of a state hospital. Diagnosis was confirmed using the M.I.N.I. Patients who met the inclusion criteria was then assessed for the severity of disease using PANSS. Smokers were given the FTND to complete. All study participants were tested using a handheld device meant to measure carbon monoxide levels in the expired air.

Results: The prevalence of smokers in was 38.1% and 73.9% of them were nicotine-dependent. Being male (OR 62.36, $p<0.01$), Malay (OR 3.03, $p<0.05$), earning more than RM500 a month (OR 0.43, $p<0.01$) and concomitant drug and alcohol abuse (OR 12.96, $p<0.01$) was significantly associated with smoking but not to nicotine dependence. No association was found between FTND scores and PANSS scores.

Conclusion: The prevalence of smoking and nicotine dependence in our study sample was very significant. It was found to be associated with higher monthly earnings.

Nicotine dependence should be included into the management of patients with schizophrenia. Specialized services are warranted to deal with this issue. Future local studies in this field are needed to address and identify other associated factors.

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CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 Schizophrenia and the burden of disease

Schizophrenia is one of the most severe and disabling of mental illnesses and the consequences of a diagnosis of schizophrenia reaches beyond the individual(1). While the incidence of the disease is considered low, it is, however, a major contributor towards the global burden of disease. This burden is largely reflected in its two features: it has its onset in early adulthood which greatly impairs personal growth and productivity, and, secondly, two thirds of individuals with schizophrenia will still suffer from persistent or fluctuating symptoms despite them being on optimal medication.

The World Health Organisation (WHO) Global Burden of Disease(2) reported that mental disorders, including schizophrenia, ranked among the 20 leading causes of disability. In 2004, WHO estimated that 16.7 million people worldwide suffered from schizophrenia. The same report showed that in all regions, neuropsychiatric conditions were the most important causes of disability, accounting for 1.1% of the total DALYs (disability-adjusted life years) and 2.8% of YLDs (years lived with disability). Among males, schizophrenia ranked fifth and among females, sixth cause of YLD (3).

1.2 Epidemiology of schizophrenia

Classically, the prevalence of schizophrenia has always been quoted as 1%(4). However, an analysis done by Saha and colleagues(5) have clearly disproved this to a lifetime prevalence of 4/1000 as opposed to the 1%. They also did not find any statistical difference in prevalence estimates between males and females. In addition, the prevalence was lower in developing nations and higher in migrants and in urban rather than rural settings.

1.3 Symptomatology of schizophrenia

The history of schizophrenia dates back to time immemorial. In his work in 1860, Morel used 'démence-précoce' to describe an early-onset state of bizarre behavior and abnormal mental function which begins in the young. Emil Kraepelin subsequently translated démence-précoce into dementia precox. Dementia precox better emphasized the disorder which involved changes in cognition (dementia) and its early onset (precox). Eugene Bleuler was the one who coined the term schizophrenia in 1911 to reflect the schisms between the thoughts, emotions and behavior present in patients with this disorder.

According to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorder fourth edition)(6), the essential features are a mixture of positive and negative symptoms which have been present for a significant portion of time over the period of a month, with some signs persisting for at least 6 months. Positive symptoms infer an excess or distortion of normal functions. Positive symptoms may be exhibited by presentations of delusions, hallucinations, and disorganized speech and behavior, whereby, in DSM-IV,

the delusions and hallucinations are grouped into the psychotic dimension and disorganized speech and behavior into the disorganization dimension. Negative symptoms, which reflect dimunition or loss in normal functioning, include affective flattening, alogia and avolition. These negative symptoms might at time cloud the clinical picture and be taken for a depressive disorder instead.

Schizophrenia is a disorder with a constellation of symptoms and no one symptom is considered pathognomonic. One of the other signs of the disorder is the presence of dysfunction in one or more areas of functioning. If the onset is in childhood or adolescence, the failure would most probably be seen in the form of not achieving what would have been expected of the individual. It could also be in the form of deterioration in function, whereby the person's functioning is below that of what was achieved before the onset of the illness.

A full blown picture of the disorder might not present itself at the onset but might be seen in the subthreshold forms of the afore-mentioned clinical symptoms. These might be either the positive or negative symptoms. These positive-like symptoms may present itself in the form of unusual beliefs but not of delusional proportions, vague perceptual experiences (e.g. sensing the presence of unseen persons), vague, digressive or overly abstract or concrete speech which might still be understandable or peculiar behavior which is not overtly disorganized. The negative symptoms may also mimic the afore-mentioned depressive-like episode.

1.4 Brief history of smoking

Tobacco was initially cultivated and smoked in pipes by the Native Americans for medicinal and ceremonial purposes. Christopher Columbus was responsible for bringing tobacco leaves and seeds back with him to Europe but it was a French, Jean Nicot who popularized its use. Nicot was an adventurer and diplomat after whom nicotine was named(7).

Tobacco was first produced for pipe-smoking, chewing and snuff. It wasn't until the early 1800s that cigars became popular. Cigarettes only became widely popular in the United States after the civil war even though crude forms of it have been available since the 1600s (7).

The early 20th century saw a growing body of evidence which addressed the negative effects of smoking. Statistical correlation has been found between smoking and cancer. However, it wasn't until an article published in the Reader's Digest in 1952 titled "Cancer by the Carton" which detailed the dangers of smoking that the smoking public began to really sit up and take notice. This was further strengthened when the Surgeon General's report on the effects of smoking on health was released in 1964. Since then, the tobacco industry has taken many hits but had managed to rise time and time again(7).

Since reports of the health hazards of smoking emerged, the tobacco industry has responded with various strategies to exert damage control. These include research into and production of cigarettes of various designs and tar contents. However, a more recent Surgeon General's report published in 2010(8) clearly stated that there is no safe cigarette. Claims of filtered, low tar and "light" variations did not actually reduce risks of disease but had in fact impaired efforts at prevention and cessation. This is because introduction

of novel tobacco products might tempt first-time smokers and delay cessation in those who should have stopped altogether. Generally speaking, it would increase morbidity in the public.

1.5 Substance use disorders (SUDs) in schizophrenia

The large Epidemiologic Catchment Area(ECA) (9) study found that nearly half of people with schizophrenia also present with a co-morbid diagnosis of substance abuse. The mechanisms underlying the high comorbidity between SUD and schizophrenia remains a poorly understood field. However, it is thought to likely include both common (across all drugs) as well as drug-specific (eg, nicotine and marijuana) factors(10).

Among those with a mental disorder, the odds ratio of having some substance use disorder was 2.7, with a lifetime prevalence of about 29%.(9) The highest substance use disorder comorbidity rate was found for those with drug (other than alcohol) disorders, 53% of whom were found to have a mental disorder. It was also discovered that individuals treated in specialty mental health and substance use disorder clinical settings have significantly higher odds of having comorbid disorders. Among the institutional settings, comorbidity of substance use disorders and severe mental disorders was highest with antisocial personality, schizophrenia, and bipolar disorders. This was especially so in the prison settings.

Substance-using schizophrenia patients were more likely to be younger and male than nonusers. Substance users had significantly more hospitalizations and more outpatient visits with positive symptoms. There was a higher rate of missed appointments

in the substance-using patients, and it correlated with hospitalizations. Substance abusers had notably more negative symptoms, except in those cases for which the alcohol user required treatment for alcoholism. Current drug use also correlated with higher tardive dyskinesia scores, higher incidence of cognitive deficiency, less education, and higher average neuroleptic dose than with non-abusers or alcohol use(11).

The local National Mental Health Registry's report between 2003-2005 found that 20% of the patients with schizophrenia had a comorbidity, with substance abuse being the commonest at 80%. Cannabis was found to be the commonest substance of abuse. However, the report did not take into account the use of nicotine in this population.

Nicotine is by far the commonest abused substance by patients with schizophrenia. In may be due, in part to its status as a licit drug and also due to its easy availability(12).

1.6 Smoking and Nicotine Dependence in Schizophrenia

Smoking remains to be the single greatest preventable cause for morbidity and mortality worldwide. The health consequences that arise from smoking are well-established and well-known to smokers but often taken lightly.

Many studies have consistently proven that smoking and nicotine dependence are highly prevalent in patients with psychiatric illnesses in general. When compared across the diagnoses, patients with schizophrenia was found to have the highest number of smokers. When compared with the general population, patients with schizophrenia were almost twice as likely to smoke(13).

Patients with schizophrenia have been found to smoke heavier, smoked cigarettes with higher tar content and smoked for longer periods. Lohr and Flynn(14) have also highlighted that these patients preferred to smoke the cigarettes until the very end, leaving evidence of this in the yellow stains frequently found on the fingers of avid smokers. This was especially seen in the institutions and with chronic mentally ill patients. The behavior of letting cigarettes burn till the end is reinforced by the finding that nicotine levels are highest at the end of these cigarettes(15).

A meta-analysis of worldwide studies of schizophrenia and tobacco smoking behaviours(16) found that the prevalence of current smoking among patients with schizophrenia was 62%. This association was consistent among the 42 samples in 20 nations included in the meta-analysis. It also found a world average odds ratio of 5.3 for current smoking in this group of patients when compared with the general population. This meta-analysis involved studies with both inpatient and outpatient samples.

Hughes et al's study(13) conducted among psychiatric outpatients found that the prevalence of smoking among the 277 subjects was 52% with the highest numbers found in patients with schizophrenia(88%) and mania (70%). This was also supported by another study performed in an outpatient clinic of an urban mental health center(17) which found that 74% of the 78 subjects with schizophrenia were current smokers.

A Singaporean study done among Chinese patients with schizophrenia who smoked(18) found a relatively high rate of smoking (31.8%) compared to a rate of 16% in the whole of the Chinese population in Singapore. However, the rate described contrasted sharply with the higher rates found in Western studies due to vigorous anti-

smoking campaigns mounted by the Singaporean authorities. There were also laws enacted in Sinagapore that made smoking illegal for people under 18 years of age.

A study conducted in Japan on 172 patients with schizophrenia found that 40.7% of them smoked. This study involved inpatients in a suburban psychiatric hospital in Tokyo. The hospital had a smoking room on each floor where the patients were allowed to smoke, but only ready-made cigarettes(19). Although the prevalence was lower than a previously done study in Japan, it was still consistent with other earlier studies that reported extraordinarily high prevalences of smoking in schizophrenia patients (13, 17, 20).

Although no difference was found between psychiatrically ill smokers and non-smokers with regards to socioeconomic status and gender composition(16), in the general population smoking is more prevalent among men and in the lower socioeconomic strata. Several factors that have been found to be related to smoking behaviour in patients with schizophrenia include male sex, youth or old age, polydipsia, early onset, high number of previous hospitalisations and high doses of antipsychotic medications(17, 21).

Researches into smoking have now turned instead to nicotine dependence, as nicotine has been found to be the most addictive substance found in tobacco. In most cases, addiction to nicotine drives people to smoke everyday in order to avoid unpleasant withdrawal symptoms. DSM-IV's core criteria for a mental disorder states : 'clinically significant behavioural or psychological syndrome or pattern that occurs in an individual and associated with distress, disability and a significantly increased risk of suffering death and disability'(4). Therefore, nicotine dependence fulfills this criteria. Low rates of remission associated with nicotine dependence is very low, cited as less than 2-3% per

year in the United Kingdom(22). It has been considered the most prevalent mental disorder and would usually last for decades once dependence has been established.

Even though literature on smoking is easily obtained, few had actually been on studies of the prevalence of nicotine dependence. Only for the past few years have research turned from smoking to nicotine dependence(23). Most large epidemiologic studies on drug or substance dependence had excluded nicotine dependence. The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (24), for instance, which was conducted in the United States examined nicotine dependence and psychiatric disorders but did not explore nicotine dependence in patients with psychotic disorders.

DSM measures for nicotine dependence had not beeen as widely used as compared to non-DSM measures in the field of tobacco research(25). DSM focused more on impaired control over drug use and physical dependence. Several other instruments, for example the Fagerstrom Test for Nicotine Dependence (FTND) also studied amount of cigarettes used and craving. The DSM measures had also undergone much lesser tests of validation as compared to the non-DSM measures(25).

Several studies which used the FTND had classified nicotine-dependent patients as being mildly dependent, highly dependent and very highly dependent(26, 27). However, for the purpose of prevalence studies, a dichotomous definition would be more appropriate as it allowed the use of logistics regression to compare patients with schizophrenia who are nicotine dependent with a control group(16). Patkar et al(28) and Solty et al(29) both used the FTND to find the prevalence of nicotine dependence in their group of patients with schizophrenia. Both these studies dichotomized their patients into

dependent and non-dependent smokers. However, their study was conducted in the inpatient setting and found a prevalence of 75.9% and 47.5% each.

In the past, the success of tobacco control programs were based only on changes in smoking prevalences(30). A study done by Breslau et al (23) which was published in 2001, found that there was a decline in the prevalence of daily smoking in persons aged 18 to 24 years old during the period studied. However, the numbers needed a more careful perusal where nicotine dependence was concerned. The same study found that the prevalence of nicotine dependence among the young daily smokers increased at a higher rate than the decline in the prevalence of smokers among the young adults. This study proved that examining smoking alone was not sufficient without taking nicotine dependence into consideration. In can be inferred that by ignoring dependence, wrong conclusions may be drawn. More importantly, the problem of nicotine dependence would not be recognized in those group of people who needed it most(31).

In a study which compared nicotine dependence in patients with schizophrenia versus mood disorders, it was found that the odds of a patient having a high nicotine dependence was 2.8 times higher than controls(32). The same study found that the odds ratio for a patient with schizophrenia to have high nicotine dependence was 2.6 as compared to controls and 3.3 for mood disorders. Gurpegui et al. (33) found a higher prevalence of high nicotine dependence in schizophrenia outpatient smokers when compared with voluntary controls who smoked . Within the same schizophrenia sample, high FTND (Fagerstrom Test For Nicotine Dependence) scores were associated with poor outcome of schizophrenia (27).

Patients with schizophrenia who smoked also smoked heavier than the general population. Most studies defined heavy smoking as smoking at least 30 sticks or 1.5 packs of cigarettes per day (16). Cigarettes are considered very effective tools which delivered nicotine to the brain. To avoid withdrawal symptoms patients associate with nicotine withdrawal, they tend to keep the number of cigarettes smoked in a day at a constant number. Therefore the number of cigarettes smoked in a day can be considered as a gross and stable indicator of smoking severity and nicotine dependence. This was reflected in a study conducted in Nithsdale, Scotland(34) that found 68% of patients in their sample, compared with 11% found in general population samples, smoked at least 25 cigarettes per day.

Studies have also found low cessation rates in people with schizophrenia. When 6 studies from 5 countries were combined, it was suggested that smoking cessation rates were smaller in patients with schizophrenia, at 9% versus between 14% and 49% for the general population (16).

Schizophrenia patients also initiated smoking at the same rate as when they were in their teens (32) even after they were 20 yrs of age while, in the control population, smoking initiation had decreased. This is in line with the hypothesis that some people who are vulnerable to schizophrenia became smokers later on in their 20s when other people rarely initiate smoking. Several studies have also reported that the proportion of patients who started smoking before the onset of illness was relatively high, ranging between 49-90%(16). A smaller study of first-episode psychosis patients also suggested that most patients with schizophrenia who smoked started doing so prior to the onset of illness(35).

1.7 Smoking and mortality risks in patients with schizophrenia

A World Health Organization report published in 2009(36) on global health risks identified 24 mortality risk factors. The six leading risks, in order of priority were high blood pressure, tobacco use, high blood glucose, physical inactivity, overweight and obesity and high levels of cholesterol. These factors combined were responsible for increasing the risk for chronic disease and were accountable for 42.1% of global mortality. However, there were variations with regards to the importance of these risk factors across countries and income groups. Therefore, an understanding of the role that these risks play is important when planning strategies to improve global health.

The association between severe mental illness and increased rates of mortality is a fact of great concern and, in fact, long recognized and scrutinized. Since early 20th century, the increase in mortality rates, more specifically in the group of disorders now labeled as schizophrenia have been under examination. Kilbourne et al (37) reported that in economically developed countries, people with schizophrenia died 20-25 years prematurely. Cancer, respiratory disease, heart disease and digestive disease are the main perpetrators of the reduction in life span (38). These causes are actually similar as those seen in the general population.

The increasing number of studies which addressed mortality rates in people with schizophrenia has enabled the calculation of standardized mortality ratio (SMR) due to the availability of data for the general population. SMRs are calculated by dividing the observed mortality rates in a given population (eg number of deaths in a group of individuals with schizophrenia) by the expected mortality rates in that same group as predicted by age- and sex-specific mortality rates for a standard population(39). It was

found that the relative mortality risks associated with schizophrenia was on the rise and that the SMRs which was examined over the past 3 decades also increased in a linear fashion(39). This indicated that even though there was increased awareness and detection of psychotic disorders and more specifically schizophrenia, certain areas of care still needed to be developed and addressed. This included the evaluation and management of smoking and nicotine dependence. The same systematic review found that even though suicide contributed to the increased mortality associated with schizophrenia, the increased rates is also attributed to other numerous somatic conditions.

The WHO report (36) highlighted that smoking and tobacco to be the second most important global risk factor, the top being hypertension. According to the report, tobacco accounted for 8.7% deaths globally. As mentioned before, several studies (36, 38) consistently showed that the rates of smoking is 2-3 times more than the general population. More alarmingly, it has also been found that for patients with schizophrenia aged 34-54 years old, the odds for a cardiovascular-related death in smokers was 12 times increased as compared to non-smokers(40). A meta-analysis conducted by Catts et al (41) found that the incidence of lung cancer in patients with schizophrenia was significantly higher than in the general population. However, after adjusting for smoking prevalence, this significance diminished, which suggested that smoking was the main factor explaining the high prevalence of lung cancer in patients with schizophrenia. The rate of cancer deaths in schizophrenia smokers was also approximately doubled(42),which again indicated that the hazardous effects of smoking cannot be pushed aside.

As was mentioned before, schizophrenia is a debilitating illness that exerts many biological, psychological and social effects on patients. Being also nicotine

dependent may increase morbidity further due to its effects on the various organ systems, mainly cardiovascular and pulmonary.

1.8 Neurobiology and Pharmacology of nicotine

Nicotine is known to affect cognition and behavior. Cigarette smoke contains more than 7,000 chemicals and compounds(43). Hundreds are toxic and at least 69 cause cancer. Tobacco smoke itself is a known human carcinogen. Nicotine, however, remains as the most addictive. There have been many reports on the effects of nicotine and variations regarding individual responses to nicotine. However, not all individuals who have a history of exposure to nicotine will get addicted to it, therefore raising the question and the possibility that response and dependence on nicotine might be genetically determined(44).

Tobacco has long been considered the most widely used method for the delivery of nicotine and therefore, the most addictive. Upon inhalation of cigarette smoke, nicotine is rapidly absorbed into the circulation and act on almost all physiological systems in the body(44). Nicotine, which is a tertiary amine, mediates its effects via the activation of different subtypes of nicotine acetylcholine receptor (nAchR)(45). The interaction between nicotine and various nAchR will facilitate the release of various neurotransmitters which include acetylcholine, dopamine, noradrenaline, serotonin, γ-aminobutyric acid (GABA) and glutamate, all of which were implicated in psychiatric disorders.

Antipsychotic drugs block postsynaptic dopamine D2 receptors and patients with schizophrenia taking antipsychotic medication may smoke to restore the blocked dopamine effects. Thus, there may be reduction of common side effects, including extrapyramidal symptoms. In addition, this attenuation of side-effects may be achieved via the induction of enzymes, namely P450 1A2 isoform (CYP1A2) and UDP-glucoronyltransferase caused by enzyme synthesis and is fully present 2 weeks after a person starts smoking and reversed 2-4 weeks after termination of smoking (46). This translates into decreased plasma levels of many typical and atypical antipsychotics (e.g. haloperidol, chlorpromazine, olanzepine and clozapine) by approximately one-third(46). It is therefore a finding that patients with schizophrenia who smoked heavily might be undertreated and might partly explain the observation that they had higher numbers of hospitalizations and more positive symptoms during acute relapses(47).

1.9 Why do patients with schizophrenia smoke?

Despite all the evidence that point towards the many health hazards and even high costs of smoking, the prevalence of schizophrenics smokers is still high.

The explanations of why there is an elevated prevalence of smoking among people with severe mental illness is likely to include neurological, psychological, behavioural and environmental factors.

Smoking has been found to exert multiple cognitive and behavioural effects even among non-psychiatric patients. Among patients with schizophrenia, smoking was strongly associated with subjective feelings of cheerfulness, agility, alertness, concentration, calmness, relaxation, habit, settling nerves, sedative effects, control of negative symptoms and addiction (26, 48, 49).

Again and again, the question of why patients with schizophrenia smoke at the rates described by so many studies have come up. The most suggested cause for this is that nicotine served a form of self-medication. Patients self-medicate themselves with nicotine to reduce the side-effects of medication, to enhance the therapeutic effects of antipsychotics and so reduce negative symptoms, and/or to improve cognitive deficits linked to schizophrenia. In addition, cigarette smoking has also been linked to familial vulnerability to schizophrenia(44).

Studies have found that smokers on antipsychotic medication displayed less medication-induced parkinsonism (17, 50). In the two studies concerned, the findings were independent of age, gender and use of anticholinergics. Goff et al (17) also found the reduced frequency of neuroleptic-induced parkinsonism in the face of smoking in this group of patients impressive as they were also on twice as high of doses of

antipsychotics. It had been established that there were excipients in the tobacco smoke which induced the hepatic enzyme and thus increased the metabolism of antipsychotics. Subsequently, the blood levels of these antipsychotics will fall. The treating psychiatrists will be expected to increase the dosage of their patients' antipsychotics in response to the psychopathology exhibited by their patients. Therefore, to control this confounding effect of nicotine-induced activation of hepatic microsomal enzymes, nicotine patches have been used to investigate the association between medication-induced extrapyramidal side-effects and nicotine(51). In this particular study which involved patients treated with haloperidol, it was suggested that nicotine can produce clinically detectable improvements in bradykinesia-rigidity.

There have also been studies which addressed response of smoker with treatment-resistant schizophrenia to clozapine. Studies have found that upon switching from a typical antipsychotic to clozapine, these patients smoked less, suggesting that the removal of the pharmacologic actions of dopamine of the conventional antipsychotic had some contribution to this effect(52).

Empirical clinical data have also shown that smoking can reduce negative symptoms without affecting the positive symptoms in patients with schizophrenia, which reflects nicotine's ability to raise dopamine levels in the nucleus accumbens and prefrontal cortex(44). Reduction of negative symptoms for example social and emotional withdrawal through either psychosocial or neurochemical actions might increase patients' social interaction with others, therefore reduce feelings of isolation and further reinforce nicotine use(48).

People with schizophrenia are known to suffer from multiple sensory processing deficits which , include auditory sensory processing (P50 deficits), eye-tracking deficits, pre-pulse inhibition abnormalities (prepulse deficiencies will lead to sensory over-stimulation and behavioural confusion) and cognitive deficiencies, all of which they smoke in order to self-medicate and improve these deficiencies. The loci for several nicotinic receptors through which nicotine acts have been genetically linked to both smoking and schizophrenia. One such receptor, α7* has been implicated in sensory gating deficits and is considered precious for cognitive functions. However, smoking desensitizes this important receptor. In a groundbreaking research conducted by Leonard et al(53), an α7* agonist tested helped to improve P50 gating and cognition, which opened new grounds for research into cholinergic nicotinic drugs. In addition, nicotine was found to enhance visuospatial working memory and attentional deficits in patients with schizophrenia who smoke(54).

CHAPTER 2: RATIONALE OF STUDY AND OBJECTIVES

2.1 Rationale of study

There is an abundance of literature pertaining to nicotine dependence. However, there is a paucity of local data regarding smoking and nicotine dependence in patients with schizophrenia in Malaysia.

In times when substance abuse and dependence are of major concern, nicotine dependence also needs due consideration. Studies in this area will help in the planning of programs dealing with smoking cessation. More specifically, it will help to target certain groups of patients identified as being at risk. Subsequently, it will help in planning health management programs and providing better, all-rounded care for patients with schizophrenia.

2.2 General objective

To quantitatively assess the prevalence and associated factors of nicotine dependence and severity of illness in outpatients with schizophrenia in Hospital Tuanku Ja'far, Seremban (HTJS).

2.3 Specific objectives

1. To determine the prevalence of smoking among outpatients with schizophrenia who smoke in HTJS.
2. To determine the prevalence of nicotine dependence among outpatients with schizophrenia who smoke in HTJS.
3. To determine the factors associated with smoking and nicotine dependence in outpatients with schizophrenia in HTJS
4. To investigate the association between smoking and nicotine dependence with the severity of illness in patients with schizophrenia in HTJS

CHAPTER 3: METHODS

3.1 Study setting

Hospital Tuanku Ja'afar, Seremban (HTJS), Negeri Sembilan is the main general hospital which is also the main tertiary hospital in Negeri Sembilan receiving referrals from other hospitals in the state. HTJS is the only hospital in Negeri Sembilan providing inpatient psychiatric services. HTJS psychiatric department covers the district of Seremban which, according to a recent census, has a population of almost 1 million. In addition, the HTJS psychiatric services also extend to the other districts in the state of Negeri Sembilan. Its services also cover areas such as Branang and Sepang in Selangor.

The Department of Psychiatry and Mental Health, HTJ is located 1.5 km from the main hospital building. The department currently houses 2 main buildings, 1 meant for the outpatient clinic and occupational therapy unit and another for the wards.

The outpatient clinic of the department runs from Monday to Friday, with Tuesdays and Thursdays allocated for follow-up cases and Mondays, Wednesdays and Fridays reserved for new cases. All cases are appointment-based. On clinic days, cases will be registered by the staff manning the registration counter. On average, a follow-up clinic day may record between 100-160 patients with a mixture of psychiatric diagnoses. 50-60% of them would meet a diagnosis of schizophrenia.

3.2 Study design

This is a cross-sectional study which was conducted in the outpatient psychiatric clinic in HTJS between August 2011 to November 2011. Follow-up cases with a diagnosis of schizophrenia were identified during registration by reviewing the case records.

3.3 Sample collection

The study population included all patients with schizophrenia who attended the outpatient psychiatric follow-up clinic of Hospital Tuanku Ja'afar, Seremban, during the study period and who met the inclusion criteria.

3.3.1 Sample size calculation

The sample size was determined by using the following formula:

$$n = \frac{Z^2 \, P(1-P)}{d^2}$$

$$= \frac{1.96^2 \text{ X } 0.8 \, (1-0.8)}{0.05^2}$$

$$= \frac{3.8416 \text{ X } 0.8 \, (0.2)}{0.0025}$$

$$= 245.8624$$

In the formula shown :

n = required sample size

Z = confidence level at 95% (given a standard value of 1.96)

P= estimated prevalence of schizophrenic patients who smoke

d = margin of error at 5% (given a standard value of 0.05)

Therefore, the targeted sample size was estimated to be 250 patients with schizophrenia. The estimated prevalence (p) was obtained by previous studies done on outpatients with schizophrenia, which have found prevalences of up to 88%(13). Therefore, for this study, p was taken as 0.8 or 80%.

3.3.2 Sampling and data collection

This study utilized the universal sampling method. Patients attending the outpatient psychiatric clinic of HTJS were screened for suitability of recruitment into the study. Patients with a clinical diagnosis of schizophrenia were administered the Mini International Neuropsychiatric Interview (M.I.N.I). If they fulfilled the inclusion criteria and did not meet any of the exclusion criteria, they would be invited to join the study. They would be given an explanation regarding the study and a written informed consent was obtained from each subject should they agree to participate.

Upon obtaining consent from the subjects, demographic and clinical data were collected. This was done via interview and information regarding previous hospitalizations and medication was obtained from the patient's case notes. The Positive and Negative Symptom Scale (PANSS) was used to rate the severity of illness in these subjects. To rate the severity of nicotine dependence, the patients who smoked were given the Fagerstrom Test for Nicotine Dependence (FTND), either the Malay or English version, to complete. The interview was completed by asking the subjects to perform a

simple breath test that will measure the levels of carbon monoxide contained in the expired air.

A total of 200 patients were approached over the study period. 19 patients were excluded from the study. Among the reasons for exclusion were due to language barrier, patients were too psychotic or disorganized and patients' refusal to participate. Therefore, a total of 181 subjects were enrolled.

3.3.3 Inclusion criteria

1. Patients diagnosed with schizophrenia by using the DSM-IV criteria for schizophrenia.
2. Patients aged above 18 years old who consented to participate in the study.
3. Patients and family who are able to understand the materials presented and communicate any concerns or questions that they have.

3.3.4 Exclusion criteria

1. Patients who refused to participate in the study.
2. Patients in whom the psychiatric symptoms are due to an acute medical illness.
3. Patients who are unable to converse in Malay or English.
4. Patients who chew tobacco.
5. Patients who are too psychotic or who are unable to coperate.

3.4 Study instruments

3.4.1 Mini International Neuropsychiatric Interview (M.I.N.I) version 6.0.0

The Mini International Neuropsychiatric Interview (M.I.N.I.) is a short, structured diagnostic interview to meet the needs for a short but accurate diagnostic tool for trials and epidemiological studies. It was developed to assess for current and lifetime psychiatric disorders according to the DSM-IV (Diagnostics and Statistical Manual for Mental Disorders fourth edition) and ICD-10 (International Classification of Disease tenth edition)criteria. It takes approximately 15-20 minutes to administer, which is less than the time taken with SCID (Structured Clinical Interview for DSM-IV Disorders), CIDI (Composite International Diagnostic Interview) or SCAN (Schedules for Clinical Assessment in Neuropsychiatry).

M.I.N.I contains 16 modules and in this study, the diagnostic category K was used. Category K deals with delusions, hallucinations, disorganized or catatonic behavior and negative symptoms. It also contains questions pertaining to Mood Disorders with or without Psychotic Features. The M.I.N.I. has been translated into many different languages and has been proven to have good reliability and validity(55).

3.4.2 Positive and Negative Syndrome Scale (PANSS)

The Positive and Negative Syndrome Scale (PANSS) is a scale which was developed to specifically assess the positive and negative symptoms of schizophrenia and also general psychopathology. It contains 30 items, 7 of which are on positive symptoms, 7 on negative symptoms and 16 on general psychopathology. PANSS is actually a combination of 18 items of the Brief Psychiatric Rating Scale (BPRS) and 12 items of the

Psychopathology Rating Schedule. All of the 30 items in PANSS are given a complete definition for ease of use. In addition, each rating point is also given a detailed anchoring. It is typically administered by clinicians who evaluate patients' current severity level on each rating point by endorsing 1 of 7 weights from absent to extreme. It has demonstrated high internal reliability and good construct validity(56).

3.4.3 Fagerstrom Test for Nicotine Dependence (FTND)

The Fagerstrom Test for Nicotine Dependence (FTND) has been used widely to measure nicotine dependence. The FTND is actually an improved version of the Fagerstrom Tolerance Questionnaire (FTQ). The FTND was developed because FTQ had significant psychometric disadvantages. It has 6 items and the total scores can range between 0 to 10. It is a self-report questionnaire which conceptualizes nicotine dependence via physiological and behavioural symptoms(57). The need for supplementary instruments to detect the presence of nicotine dependence was supported by the fact that 39.4% did not meet the criteria for nicotine dependence even though the smoking history suggested this(58). However, this also suggests that other factors besides extensive nicotine use may play a part in order for nicotine dependence to occur.

For purposes of a time-saving estimates of degree of nicotine dependence to use in surveys, the Heavy Smoking Index or HSI was derived from two items in the FTND, namely "number of cigarettes per day" (CPD) and "time to first cigarette of the day" (TTF) which are questions one and four in the questionnaire(59). The HSI has been found to be reasonably good screening tool for daily smokers with high nicotine dependence but for the FTND was more suited for subpopulations with low nicotine dependence(60).

This study utilized both the English and Malay versions (FTND_M) of FTND. The validity and reliability of the English version of FTND has been well established(57). The validation of the FTND_M was timely as the Malay language is the most often used language in the study population. This study followed in the wake of the validated FTND_M(61). At the cut-off point of more than 2, the study by Anne Yee et al found that the FTND_M had the following properties: sensitivity of 70.1%, specificity of 70%, PPV of 79.7% and NPV of 58.3%, similar to the English version (61). The FTND_M also had good discriminatory ability and moderate internal consistency.

3.4.4 Breath Carbon Monoxide Monitor

A simple breath test that will measure the levels of carbon monoxide levels in the expired air. It is useful as a tool to obtain physiological evidence of smoking or non-smoking. Patients were instructed to hold their breaths for 20 seconds then exhale into the device. Expired air was measured for an end-tidal reading of carbon monoxide. Each patient was given 2 trials and an average of the two readings was taken. This handheld device measures %COHb . Levels ranged from non-smoker to dangerously addicted smoker.

3.5 Definition of variables

3.5.1 Smokers

Smokers refer to study participants who were current daily smokers. These were obtained via self-reports obtained by the researcher from the study participants.

3.5.2 Duration of illness

Duration of illness refers to the period starting from the point where there were non-specific symptoms and growing functional impairment even before the more specific positive psychotic symptoms had emerged(62). This period has often also been referred to as the prodrome.

3.5.3 Nicotine dependence

Nicotine dependence was diagnosed using the Fagerstrom Test for Nicotine Dependence by using a cut-off point of 2.

3.5.4 Chlorpromazine equivalent doses

Dosage of each medication and depot medication was converted to chlorpromazine equivalent dosages according to conversion tables published by previous studies(63-65).

3.6 Ethical considerations

This study was registered with the National Medical Research Registry of the Ministry of Health, Malaysia. The Ministry of Health Medical Research Ethical Committee provided the ethical approval for this study. Upon entrance into the study, the selected subjects were also required to sign a written informed consent.

3.7 Statistical analyses

Analyses of data was performed using the Statistical Package for Social Studies (SPSS) version 19.0 to generate the relevant descriptive epidemiological statistics.

The baseline characteristics of the study subjects were analysed using descriptive statistics. Univariate analyses using chi-square test and Fisher's exact test (if frequency in a cell was less or equals to 5) were performed to compare the smokers and non-smokers across all the demographic and clinical characteristics which were dichotomised accordingly. The same analysis was performed again but now with regards to nicotine dependence.

Comparison of the means of PANSS score and all its subscales and Fagerstrom scores were done using the t-test. This was done to analyse the association between disease severity and nicotine dependence with the sociodemographic and clinical characteristics of the study subjects. For all the variables found to be significant via univariate analyses, multivariate analyses was then performed using logistic regression to control for all possible confounders.

Spearman's correlation was used to analyse the association between PANSS score, its subscales and Fagerstrom scores.

P values of less than 0.05 were taken as statistically significant for the relevant tests that were performed.

CHAPTER 4: RESULTS

4.1 SOCIODEMOGRAPHIC CHARACTERISTICS

Table 1: Sociodemographic characteristics of the study participants.

Characteristics		n	%	Mean	SD
Age				41.42	11.42
Gender	Male	116	64.10		
	Female	65	35.90		
Ethnicity	Malay	83	45.10		
	Chinese	70	38.70		
	Indian	28	15.50		
Marital status	Single	122	67.40		
	Married	56	30.90		
	Divorced	3	1.70		
Current occupation					
	Professional/technical/	2	1.10		
	managerial	7	3.90		
	Military / police / fireman	2	1.10		
	Factory worker	3	1.70		
	Clerical / sales	20	11.00		
	Service	20	11.00		
	Homemaker / housewife	5	2.80		
	Own business	1	0.60		
	Student	38	21.00		
	Others	82	45.90		
	Unemployed	1	0.60		
	Retired				
Total income	≤RM500	135	74.60		
	RM501-1000	30	16.60		
	RM1001-2000	8	4.40		
	RM2001-3000	7	3.90		
	>RM3000	1	0.60		
Education level	Primary	25	13.80		
	Secondary	128	70.70		
	College / university	27	14.90		
	Nil	1	0.60		

SD = standard deviation

Out of the 200 patients approached for this study, 181 patients fulfilled the inclusion criteria and were recruited and agreed to participate. Table 1 demonstrates the sociodemographic characteristics of the study participants.

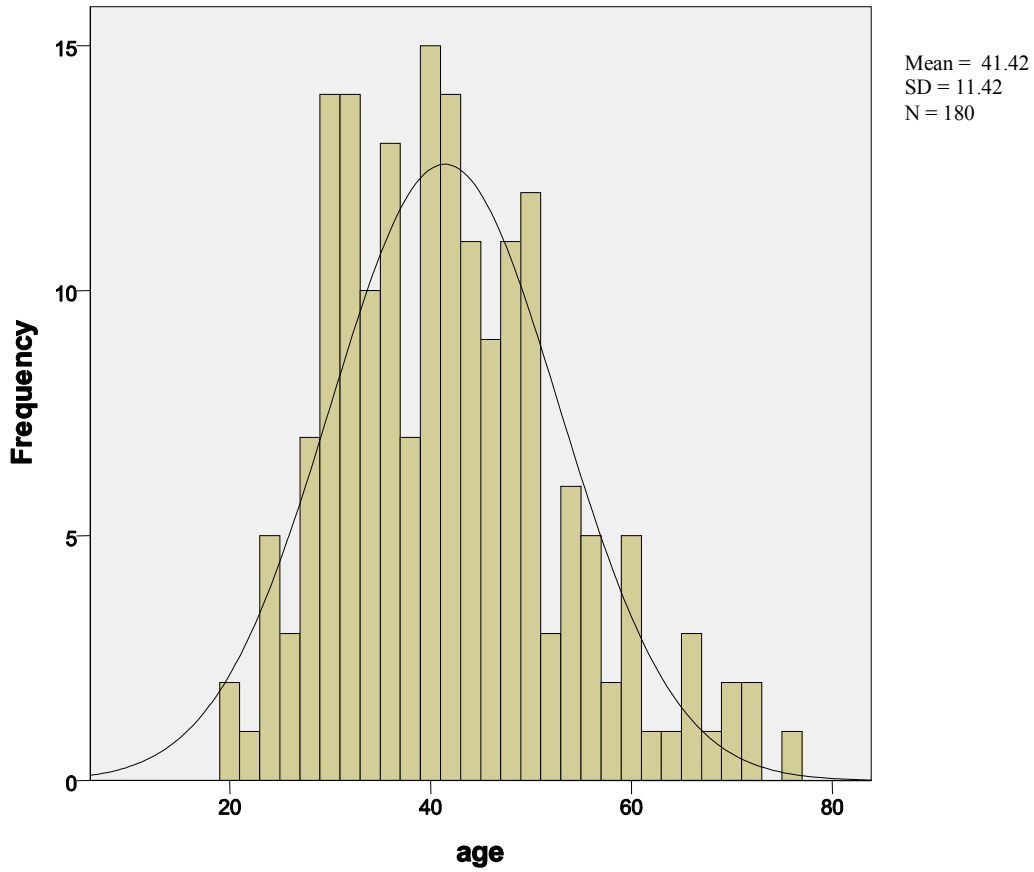
The mean age of the study participants was 41.42 years old, with a standard deviation of 11.42(Table 1). Most of them were at least 40 years old (53.6%) and the remaining 46.4% were less than 40 years of age.

Males made up 64.1% (n=116) of the study participants, and the remaining 35.9% were females. Most of the study participants (45%) were Malays, followed by 38.7% Chinese and 15.5% Indians. The majority of the study participants were single (67.4%), while 56 (30.9%) of them were divorced at the time of recruitment.

A large number of the study participants were not working at the time of interview (n=82, 45.9%). Housewives and those in the fields of service (waiter / maid / security guard) each made up another 20% of the study participants. Most of the study participants were in the low socioeconomic group, whereby 74.6% of them had a personal income of less than RM500 per month. The rest of the study participants earned more than RM500 per month. Only one participant had a personal income of more than RM3000 per month.

One hundred twenty-eight participants or 70.7% had studied until secondary school. Another 27 of them or 14.9% had went to college or university, 13.8% obtained only primary education and 1 participant did not receive any formal education.

Figure 1: Age distribution of the study participants



4.2 CLINICAL CHARACTERISTICS

Table 2: Clinical characteristics of study participants

	N	%	Mean	SD
Duration of illness (years)			14.99	10.07
Duration of smoking (years)			19.94	11.30
Age start smoking (years)			19.68	6.25
Number of cigarettes smoked			16.55	9.30
Breath CO levels				
Smokers			ppm 13.91	3.16
			COHb 3.16	2.15
Non-smokers			ppm 2.22	0.65
			COHb 1.02	0.09
Number of hospitalisations			1.73	2.63
Chlorpromazine equivalent (mg)			285.66	400.12
Total PANSS score			50.04	2.36
PANSS positive subscale score			8.98	2.97
PANSS negative subscale score			17.39	5.84
PANSS general psychopathology subscale score			23.22	5.18
Total FTND score			4.16	10.73
Oral typical antipsychotics	No	108	59.70	
	Yes	73	40.30	
Oral atypical antipsychotics	No	82	45.30	
	Yes	99	54.70	
Anticholinergic	No	48	26.50	
	Yes	133	73.50	
Depot antipsychotics	No	111	61.30	
	Yes	70	38.70	
Benzodiazepines	No	160	88.40	
	Yes	21	11.60	
Antidepressants	No	172	95.00	
	Yes	9	5.00	
Family history of smoking	No	67	37.00	
	Yes	114	63.00	

SD = standard deviation

Clinical characteristics of the study participants are as shown in Table 2.

The mean duration of schizophrenia in the participants was 14.99 years with a standard deviation of 10.07.

Those participants who smoked had been smoking for a mean of 19.94 years and they had started smoking at a range of between 10 to 43 years old, with a mean of 19.68 years (SD 6.25). The mean number of cigarettes smoked was 16.55 (SD 9.30) with a range of 2 to 40 sticks a day.

Measurements of carbon monoxide levels in the expired air using a handheld device showed that the non-smokers had levels within the acceptable range. The mean for smokers of 13.91 ppm indicated that they were addicted to nicotine.

The mean number of hospitalisations was 1.73 (SD 2.63), whereby 38.1% of the study participants had never been hospitalised.

With regards to medication use, dosage of all medications were converted to Chlorpromazine equivalent doses(63, 66). However, it was found to be not normally distributed, with a median of 200 mg/day. There were more patients on oral atypical (54.7%, n=99) antipsychotics as opposed to oral typical antipsychotics (40.3%, n=73). There were only 4 patients who were on both oral typical and atypical antipsychotics. Therefore, analysis was not performed for this variable. Seventy participants (n=38.7%) were on depot antipsychotics, all of which were the typical depot injections, namely fluphenazine decanoate, flupenthixol decanoate and zuclopenthixol decanoate. Anticholinergics were taken by 133 participants (73.5%) , 11.6% (n=21) on benzodiazepines and 9(5%) were on antidepressants.

The mean total PANSS score was 50.04 (SD = 2.36) and mean total FTND score was 4.16 (SD = 10.73).

The study also found that 37% (n=67) of the study participants had a positive family history of smoking.

Figures 2 and 3 below shows the distribution of the total PANSS and FTND scores of the study participants, both of which were found to be normally distributed.

Figure 2: Distribution of total PANSS scores among the study participants

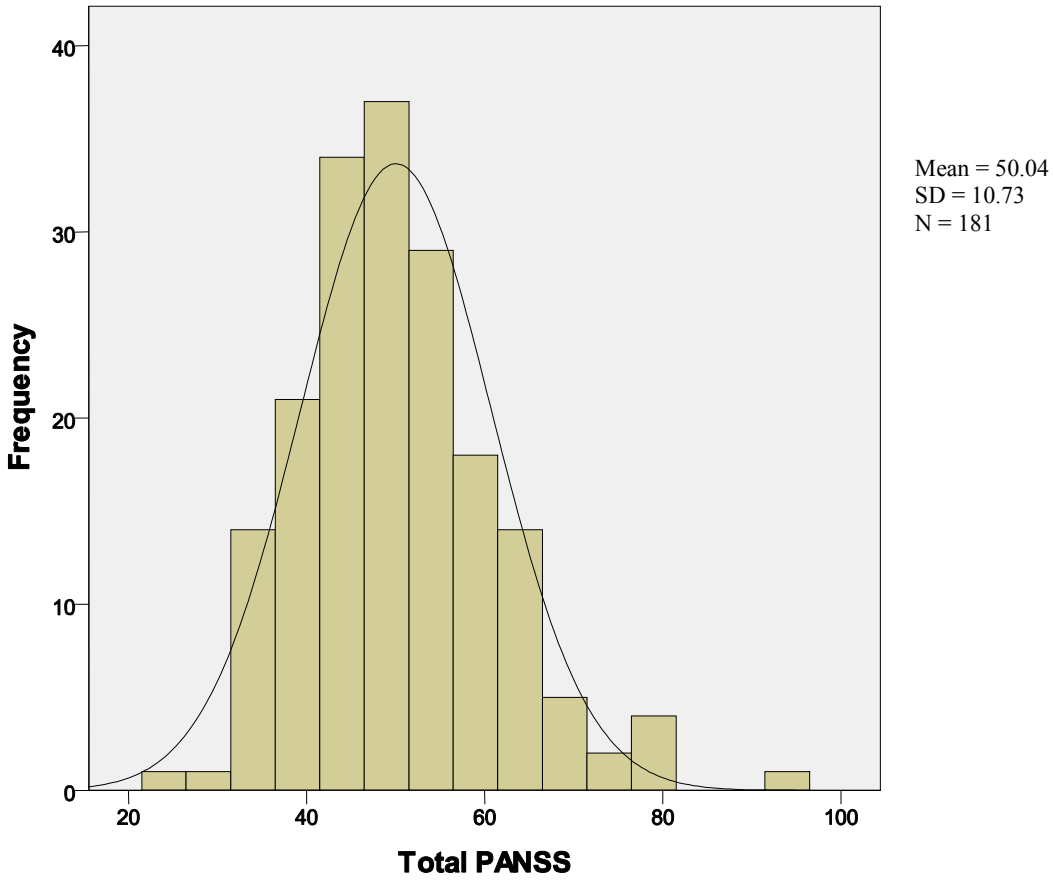
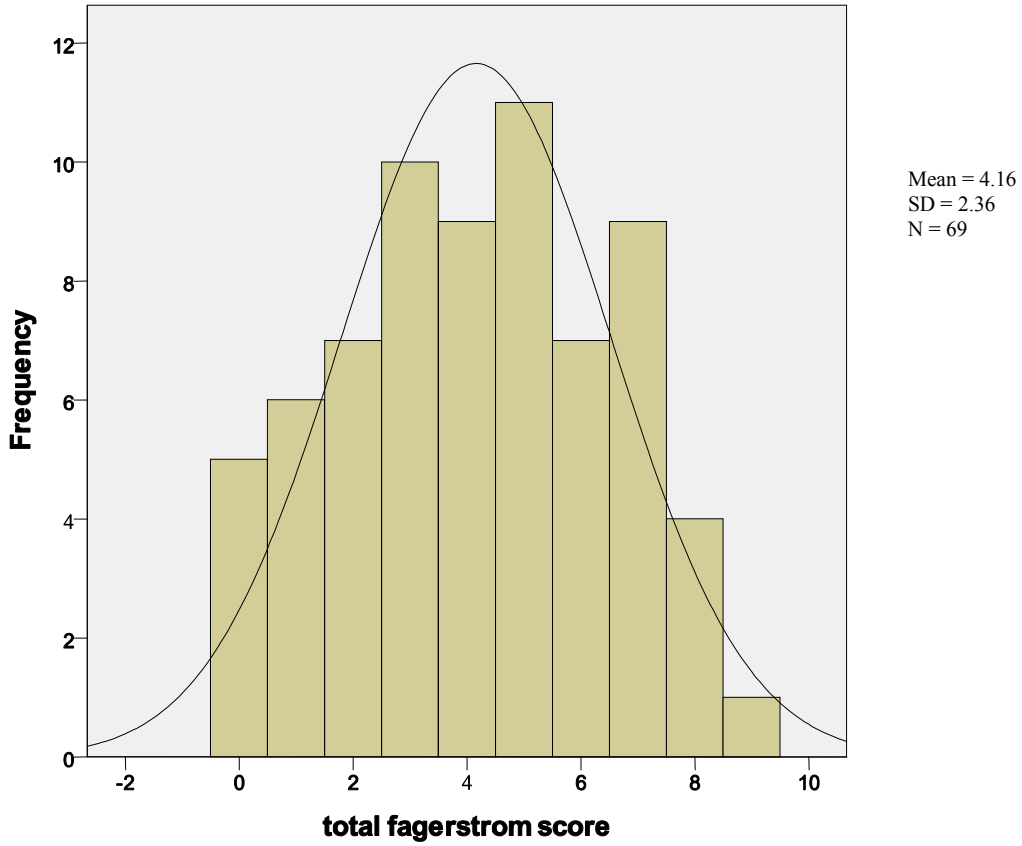


Figure 3: Distribution of total FTND scores among the study participants



4.3 PREVALENCE OF SMOKING AND NICOTINE DEPENDENCE

Table 3: Prevalence of smoking and nicotine dependence in the study participants

		N	%
Smoking status	Smoker	69	38.1
	Non-smoker	96	53.0
	Ex-smoker	16	8.8
Nicotine dependence	Yes	51	73.9
	No	18	26.1

The prevalence of smoking in the study participants was performed by asking the patients directly regarding their smoking habits. This was further confirmed by asking accompanying relatives or persons.

The prevalence of smoking in this group of patients with schizophrenia was found to be 38.1% (n=69). Non-smokers and ex-smokers accounted for the remainder 61.8% (n = 112). A sub-analysis of the participants who were currently not smoking found that 8.8% of them were actually ex-smokers.

Nicotine dependence, diagnosed using the Fagerstrom Test for Nicotine Dependence (FTND, Malay or English version) found a total of 51 or 73.9% to be dependent on nicotine. The remainder 18 study participants or 26.1% had total FTND scores of more than two and were therefore considered not dependent on nicotine.

Figure 4: Prevalence of smoking among the study participants

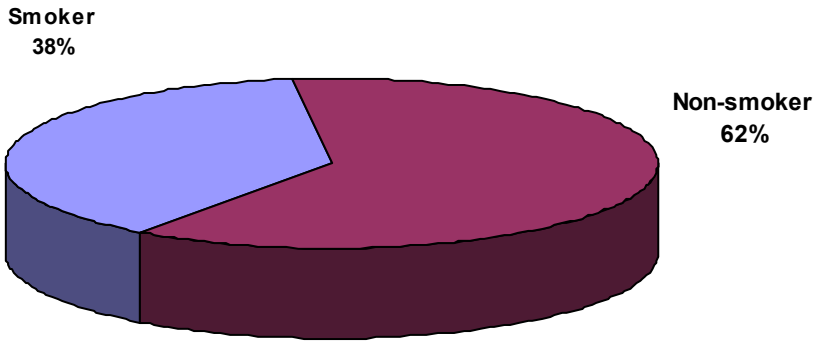
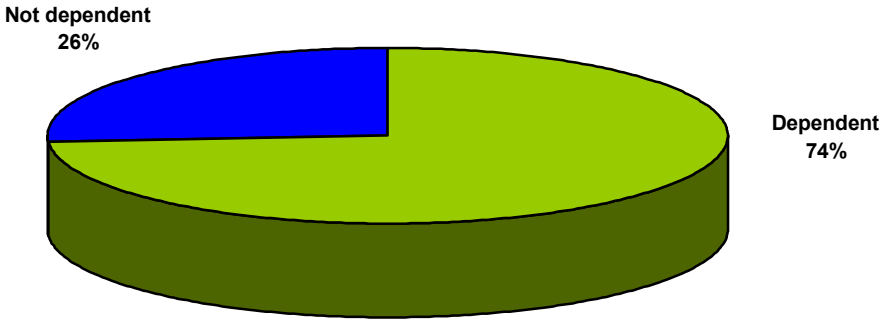


Figure 5: Prevalence of nicotine dependence among the study participants



4.4 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS, CLINICAL CHARACTERISTICS AND PANSS SCORES WITH SMOKING STATUS

Table 4: Univariate analysis of association between sociodemographic and clinical characteristics with smoking status using chi square test

	Smoking status		**Chi square**	**p value**	**OR**	**95% CI**
	Yes n(%)	No n (%)				
Age						
<40 years old	42 (50.0)	42(50.0)	9.38	p<0.01*	2.60	1.4 - 4.803
≥40 years old	27(27.8)	70(72.2)				
Gender						
Male	68(58.6)	48(41.4)	57.54	p<0.01*#	90.68	12.155 – 676.321
Female	1(1.5)	64(98.5)				
Ethnicity						
Malay	41(49.4)	42(50.6)	8.26	p<0.01*	2.44	1.32-4.51
Non-Malay	28(28.6)	70(71.4)				
Marital status						
Married	17(30.4)	39(69.6)	2.07	0.15	0.61	0.313 – 1.198
Not married	52(41.6)	73(58.4)				
Employment status						
Employed	41(42.7)	55(57.3)	1.82	0.18	1.52	0.83-2.78
Unemployed	28(32.9)	57(67.1)				
Total income						
≤RM500	43(31.9)	92(68.1)	8.85	0.03*	0.36	0.18-0.71
>RM500	26(56.5)	20(43.5)				
Education level						
Primary and below	10(38.5)	16(61.5)	0.01	0.97	1.02	0.433-2.39
Secondary / tertiary	59(38.1)	96(61.9)				
Drug and alcohol						
Yes	19(90.5)	2(9.5)	27.60	p<0.01*#	20.90	4.69 – 93.19
No	50(31.3)	110(68.8)				
Duration of illness+						
12 years or less	45(43.3)	59(56.7)	2.75	0.09	1.68	0.91-3.13
More than 12 years	24(31.2)	53(68.8)				
Number of hospitalisations						
2 or less	21(30.0)	49(70.0)	3.19	0.07	0.56	0.30-1.06
More than 2	48(43.2)	63(56.8)				

Chlorpromazine equivalent (mg)$^{+}$						
≤200mg/day	31(32.6)	64(67.4)	2.56	0.11	0.61	0.33-1.12
>200 mg/day	38(44.2)	48(55.8)				
Typical antipsychotics						
Yes	19(27.1)	51(72.9)	5.83	0.02*	0.46	0.24-0.87
No	50(45.0)	61(55.0)				
Atypical antipsychotics						
Yes	45(46.0)	53(54.0)	5.51	0.02*	2.09	1.12-3.88
No	24(29.0)	59(71.0)				
Anticholinergic						
Yes	54(40.6)	79(59.4)	1.31	0.25	1.5	0.75-3.00
No	15(31.3)	33(68.7)				
Depot antipsychotics						
Yes	32(46.4)	37(53.6)	3.22	0.07	1.75	0.95-3.20
No	37(33.0)	75(67.0)				
Benzodiazepines						
Yes	11(52.4)	10(47.6)	2.05	0.16	1.93	0.78-4.83
No	58(36.3)	102(63.7)				
Antidepressants						
Yes	1(11.1)	8(88.9)	2.93	0.87$^{\#}$	0.19	0.02-1.56
No	68(39.5)	104(60.5)				
Family history of smoking						
Yes	54(47.4)	60(52.6)	11.16	p< 0.01*	3.12	1.58 – 6.17
No	15(22.4)	52(77.6)				

*p < 0.05, # Fisher's exact test

OR = odds ratio, CI=confidence interval

In order to perform univariate analysis, variables such as age, ethnicity, marital status, employment status, total income, education level, duration of illness, number of hospitalisations and chlorpromazine equivalent dosage were dichotomized. Dichotomizing these variable would allow the calculation of odds ratio in the univariate analyses(21). All of the afore-mentioned variables were normally distributed except for duration of illness and chlorpromazine equivalent dosage.

Analysis of the sociodemographic variables showed several significant findings. Smokers were more likely to be in the younger age group (less than 40 years old, OR = 2.6). Smokers were also more likely to be male, Malays, with a total monthly income of more than RM500. Being unmarried appeared to be associated with smoking but it was not statistically significant.

Analysis of the clinical variables showed that those taking drugs or alcohol was associated with a higher prevalence of smoking. It also appeared that smokers were more likely to have been hospitalised more than twice during the duration of illness. However, it was not statistically significant.

Smokers were also found to be twice as likely to be taking atypical antipsychotics and had a 3.12 odds ratio of a family history of smoking. It also showed with statistical significance that smokers were less likely to be taking oral typical antipsychotics. They were also more likely to be associated with smoking more than 20 cigarettes per day.

Table 5: Univariate analysis of association between total PANSS score and subscale scores with smoking status using chi square

	Smoking status		Chi square	p value	OR	95% CI
	Yes n(%)	No n(%)				
PANSS total score						
<50	33(34.0)	64(66.0)	1.49	0.22	0.69	0.28-1.26
≥50	36(42.9)	48(57.1)				
PANSS positive subscale score						
<9	27(26.0)	77(74.0)	15.32	p<0.05*	0.29	0.16-0.55
≥9	42(54.5)	35(45.5)				
PANSS negative subscale score						
<17	36(41.9)	50(58.1)	0.97	0.32	1.35	0.74-2.47
≥17	33(34.7)	62(65.3)				
PANSS general psychopathology subscale score						
<23	25(27.2)	67(72.8)	9.51	p<0.05*	0.38	0.21-0.71
≥23	44(49.4)	45(50.6)				

*p <0.05, # Fisher's exact test

OR = Odds Ratio, CI = Confidence Interval

To perform this analysis, the total PANSS score and all 3 of the subscale scores were dichotomised, as shown in the table above. All of these scores were found to be normally distributed when tested using the Kolmogorov-Smirnov test.

Two PANSS subscales were found to be significantly associated with smoking status. Participants who smoked were more likely to have scored at least 9 in the positive

subscale score. Those who smoked were also more likely to score 23 or higher on the general psychopathology subscale score.

Although it appeared that the smoking participants scored higher in total on the PANSS and lower on the negative subscale, these were not statistically significant when the chi square test was performed.

Table 6: Multivariate analysis between sociodemographic, clinical characteristics and PANSS scores with smoking status among the study participants using logistics regression

	B	S.E.	P	Adjusted OR	95% C.I.
Age					
<40 years old	0.89	0.46	0.05	2.43	0.99 – 5.93
≥40 years old					
Gender					
Male	4.13	1.06	p<0.01*	62.36	7.89 – 492.89
Female					
Ethnicity					
Malay	1.11	0.46	0.02*	3.03	1.22 – 7.50
Non-Malay					
Total income					
≤RM500	-0.84	0.86	p<0.01*	0.43	0.16 – 1.17
>RM500					
Drug and alcohol					
Yes	2.56	0.86	p<0.01*	12.96	2.41 – 69.60
No					
Typical antipsychotics					
Yes	-0.81	0.80	0.31	0.45	0.09 – 2.13
No					
Atypical antipsychotics					
Yes	-0.40	0.78	0.61	0.67	0.15 – 3.08
No					
Family history					
Yes	0.17	0.50	0.73	1.18	0.45 – 3.14
No					
Total positive					
<9	-0.49	0.48	0.30	0.61	0.24 – 1.56
≥9					
Total psychopathology					
<23	-0.11	3.46	0.83	0.90	0.34 – 2.34
≥23					

*p<0.05

SE = standard error, OR = odds ratio, CI = confidence interval

Multivariate analysis between sociodemographic, clinical characteristics and PANSS scores with smoking status revealed statistically significant association between gender, ethnicity, total income earned and use of drugs and alcohol,

4.5 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS, CLINICAL CHARACTERISTICS AND PANSS SCORES WITH NICOTINE DEPENDENCE

Table 7: Univariate analysis between sociodemographic factors and clinical characteristics with nicotine dependence among smokers using chi square

	Nicotine dependence		Chi square	p value	OR	95% CI
	Yes n(%)	No n (%)				
Age						
<40 years old	30(71.4)	12(28.6)	0.34	0.558	0.71	0.23-2.21
≥40 years old	21(77.8)	6(22.2)				
Gender						
Male	51(75.0)	17(25.0)	2.88	0.26[#]	0.25	0.17-0.38
Female	0(0)	1(100.0)				
Ethnicity						
Malay	31(75.6)	10(24.4)	0.15	0.7	1.24	0.42-3.68
Non-Malay	20(71.4)	8(28.6)				
Marital status						
Married	14(82.4)	3(17.6)	0.83	0.53[#]	1.9	0.47-7.55
Not married	37(71.2)	15(28.8)				
Employment status						
Employed	31(75.6)	10(24.4)	0.15	0.7	1.24	0.42-3.68
Unemployed	20(71.4)	8(28.6)				
Total income						
≤RM500	30(69.8)	13(30.2)	1.02	0.31	0.55	0.17-1.78
>RM500	21(80.8)	5(19.2)				
Education level						
Primary and below	7(70.0)	3(30.0)	0.93	0.76	0.8	0.18-3.47
Secondary / tertiary	44(74.6)	15(25.4)				
Drug and alcohol						
Yes	16(84.2)	3(15.8)	1.44	0.23	2.29	0.58-9.03
No	35(72.9)	15(27.1)				
Duration of illness						
≤15 years	32(71.1)	13(28.9)	0.53	0.468	0.65	0.2-2.1
>15 years	19(79.2)	5(20.8)				
Number of hospitalisations						
≤2	14(66.7)	7(33.3)	0.82	0.37	0.6	0.19-1.84
>2	37(77.1)	11(22.9)				
Chlorpromazine equivalent (mg)						
≤200 mg/day	31(32.6)	64(67.4)	2.56	0.11	0.61	0.33-1.12
>200 mg/day	38(44.2)	48(55.8)				

Typical antipsychotics						
Yes	15(78.9)	4(21.1)	0.35	0.761#	1.46	0.41-5.16
No	36(72.0)	14(28.0)				
Atypical antipsychotics						
Yes	33(73.3)	12(26.7)	0.23	0.88	0.92	0.29-2.86
No	18(75.0)	6(25.0)				
Anticholinergic						
Yes	39(72.2)	15(27.8)	0.37	0.74#	0.65	0.16-2.63
No	12(80.0)	3(20.0)				
Depot antipsychotics						
Yes	25(78.1)	7(21.9)	0.55	0.46	1.51	0.51-4.52
No	26(96.3)	11(3.7)				
Benzodiazepines						
Yes	7(40.5)	4(59.5)	0.72	0.46#	0.56	0.14-2.19
No	44(75.9)	14(24.1)				
Antidepressants						
Yes	1(100.0)	0(0)	0.36	0.11#	1.36	1.18-1.57
No	50(73.5)	18(26.5)				
Duration of smoking						
<19 years	23(67.6)	11(32.4)	1.37	0.24	0.52	0.18 - 1.57
≥19 years	28(80.0)	7(20.0)				
Age start smoking						
<20 years old	31(72.1)	12(27.9)	0.20	0.66	0.78	0.25 - 2.40
≥20 years old	20(76.9)	6(23.1)				
Family history of smoking						
Yes	37(68.5)	17(31.5)	3.75	0.09#	0.16	0.19-1.28
No	14(93.3)	1(6.7)				

*p <0.05, # Fisher's exact test

OR = Odds Ratio, CI = Confidence Interval

Results of the analysis to find an association between participants' sociodemographic and clinical characteristics with nicotine dependence are shown in Table 7. However, no variables were found to statistically significant with nicotine dependence.

Table 8: Univariate analysis of association between total PANSS score and subscale scores with nicotine dependence using chi square

	Nicotine dependence		Chi square	OR	Adjusted OR	95% CI for Adjusted OR	p value
	Yes n(%)	No n(%)					
PANSS total score							
<50	33(34.0)	64(66.0)	1.49	0.68	0.79[a]	0.24 – 2.57	0.69
≥50	36(42.9)	48(57.1)					
PANSS positive subscale score							
<9	27(26.0)	77(74.0)	15.32	0.29	0.47[a]	0.15 – 1.50	0.20
≥9	42(54.5)	35(45.6)					
PANSS negative subscale score							
<17	36(41.9)	50(58.1)	0.97	1.35	1.12[a]	0.35 – 3.62	0.85
≥17	33(34.7)	62(65.3)					
PANSS general psychopathology subscale score							
<23	25(27.2)	67(72.8)	9.51	0.38	1.04[a]	0.32 – 3.38	0.95
≥23	44(49.4)	45(50.6)					

Fisher's exact test, * $p<0.05$

[a] Adjusted for gender, ethnicity, total income and drug and alcohol

OR = Odds Ratio, CI = Confidence Interval

Table 8 depicts the results of the univariate analysis which was performed to find the association between total PANSS score and the 3 subscale scores with nicotine dependence.

Statistically significant association was found between the PANSS positive subscale score and PANSS general psychopathology subscale score with nicotine dependence. Scores of 9 or more on the positive subscale and 23 or more on the general psychopathology subscale were associated with nicotine dependence.

Even though no significant association was found between any of the sociodemographic and clinical characteristics of the study participants with nicotine dependence, multivariate analysis was performed with the variables found significant with regards to smoking status (refer to Table 6).Each of the PANSS total score, PANSS positive, negative and general psychopathology subscale scores were adjusted for gender, ethnicity, total income and drug and alcohol use. However, no statistically significant findings were obtained.

4.6 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS, CLINICAL CHARACTERISTICS AND PANSS SCORES WITH TOTAL FTND SCORES

Table 9: Analysis of association between sociodemographic and clinical characteristics with total FTND scores using t-test

	Mean (SD)	Mean difference	t	P	95%CI
Age					
<40 years old	3.86(2.15)	-0.77	-1.33	0.19	-1.93-0.38
>40 years old	4.63(2.66)				
Gender					
Male	4.21(2.35)	3.21	1.36	0.18	-1.51-7.93
Female	1.00				
Ethnicity					
Malay	4.34(2.19)	0.45	0.77	0.44	-0.71-1.61
Non-Malay	3.89(2.62)				
Marital status					
Married	4.35(2.06)	0.26	0.39	0.70	-1.07-1.58
Not married	4.10(2.47)				
Employment status					
Employed	4.24(2.38)	0.21	0.36	0.72	-0.96-1.37
Unemployed	4.04(2.38)				
Total income					
≤RM500	3.93(2.34)	-0.61	-1.04	0.30	-1.78-0.56
>RM500	4.54(2.39)				
Education level					
Primary and below	4.00(2.71)	-0.19	-0.23	0.82	-1.81-1.44
Secondary / tertiary	4.19(2.32)				
Drug and alcohol					
Yes	4.74(2.38)	0.80	1.26	0.21	-0.47-2.06
No	3.94(2.34)				
Duration of illness					
12 years or less	3.58(2.07)	-1.39	-2.51	0.02*	-2.50- -0.28
More than 12 years	4.97(2.53)				
Number of hospitalisations					
2 or less	3.57(1.99)	-0.85	-1.38	0.17	-0.27-0.38
More than 2	4.42(2.48)				
Chlorpromazine equivalent (mg)					
≤200 mg/day	3.61(2.19)	-0.99	-1.76	0.08	-2.12-0.13
>200 mg/day	4.61(2.43)				

Typical antipsychotics					
Yes	4.53(2.61)	0.51	0.79	0.43	-0.77-1.78
No	4.02(2.27)				
Atypical antipsychotics	4.13(2.32)	-0.08	-0.125	0.90	-1.275-1.12
Yes	4.21(2.48)				
No					
Anticholinergic					
Yes	4.11(2.38)	-0.22	-0.32	0.75	-1.61-1.16
No	4.33(2.35)				
Depot antipsychotics					
Yes	4.31(2.44)	0.29	0.50	0.62	-0.86-1.43
No	4.03(2.32)				
Benzodiazepines					
Yes	3.82(2.68)	-0.41	-0.52	0.61	-1.97-1.15
No	4.22(2.32)				
Antidepressants					
Yes	6.00	1.87	0.78	0.44	-2.89-6.63
No	4.13(2.34)				
Family history of smoking					
Yes	3.93(2.40)	-1.07	-1.58	0.12	-2.44-0.29
No	5.00(2.07)				

* $p < 0.05$

SD= standard deviation, CI = Confidence Interval

After running the t-test for association between sociodemographic and clinical characteristics with total FTND scores, only one variable was found to be statistically significant. Study participants who had been ill for more than 12 years was found to be associated with higher total FTND scores (mean 4.97 SD 2.53).

Participants who had been hospitalised more than twice in the past, were on more than 200 mg/day of chlorpromazine equivalent dose of medication and those without a family history of smoking seemed to have higher FTND scores but these were not statistically significant.

Table 10: Analysis of association between total PANSS score and subscale scores with total FTND score

	Mean (SD)	Mean difference	T	p	95% CI
Total PANSS score					
<50	4.03(2.35)	-0.247	-0.43	0.67	-1.39-0.90
≥50	4.28(2.40)				
Total positive subscale score					
<9	3.74(2.58)	-0.69	-1.18	0.24	-1.85-0.47
≥9	4.43(2.20)				
Total negative subscale score					
<17	4.25(2.26)	0.19	0.33	-0.47	-0.95-1.33
≥17	4.06(2.50)				
Total general psychopathology subscale score					
<23	4.12(2.28)	-0.062	-0.14	0.92	-1.25-1.13
≥23	4.18(2.43)				

SD= standard deviation, CI= confidence interval

Analysis of association between PANSS scores and smoking status revealed that smoking was associated with higher scores on the positive subscale and general psychopathology subscale scores. However, this association was not seen when the same analysis was performed with nicotine dependence. There was also no association with the other two subscales.

4.7 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS AND CLINICAL CHARACTERISTICS WITH PANSS TOTAL SCORES

Table 11: Association between sociodemographic and clinical characteristics with total PANSS score using t-test

	PANSS Mean(SD)	Mean diff	t	P	95% CI
Age					
<40 years old	51.74(11.37)	3.17	2.00	0.05	0.42-6.30
>40 years old	48.57(9.96)				
Gender					
Male	51.42(11.60)	3.85	2.35	0.02*	0.61-7.09
Female	47.57(8.50)				
Ethnicity					
Malay	49.73(11.74)	-0.56	-0.35	0.73	-3.73 – 2.60
Non-Malay	50.30(9.84)				
Marital status					
Married	46.11(9.59)	-5.69	-3.40	p<0.01*	-9.00- -2.39
Not married	51.80(10.78)				
Employment status					
Employed	47.83(9.182)	-4.70	-3.01	p<0.01*	-7.780- -1.162
Unemployed	52.53(11.81)				
Total income					
<RM500	50.96(10.93)	3.64	2.00	0.04*	0.05-7.22
>RM500	47.33(9.73)				
Education level					
Primary and below	48.77(8.83)	-1.48	-6.51	0.52	-5.98-3.01
Secondary / tertiary	50.25(11.023)				
Drug and alcohol					
Yes	53.86(9.86)	4.32	1.75	0.08	-5.65-9.20
No	49.54(10.76)				
Duration of illness					
15 years or less	50.01(11.01)	-0.06	-0.04	0.97	-3.21-3.10
More than 15 years	50.07(10.49)				
Number of hospitalisations					
2 or less	46.97(10.42)	-5.00	-3.13	p<0.01*	-8.16- -1.85
More than 2	51.00(10.51)				
Chlorpromazine equivalent (mg)					
≤200 mg/day	48.83(10.42)	-2.54	-1.60	0.11	-5.68 – 0.60
>200 mg/day	51.37(10.96)				
Typical antipsychotics					
Yes	47.54(9.37)	-4.07	-2.52	0.01*	-7.25- -0.89
No	51.61(11.26)				

Atypical antipsychotics					
Yes	51.97(11.69)	4.21	2.68	0.01*	1.11-7.32
No	47.76(9.01)				
Anticholinergic					
Yes	50.76(10.14)	2.72	1.51	0.13	-0.834- 6.27
No	48.04(12.11)				
Depot antipsychotics					
Yes	50.26(10.81)	0.36	0.22	0.83	-2.90-3.61
No	49.90(10.73)				
Benzodiazepines					
Yes	51.24(8.13)	1.36	0.54	0.59	-3.57-6.28
No	49.88(11.03)				
Antidepressants					
Yes	52(13.90)	2.06	0.56	0.58	-5.19-9.32
No	49.94(10.58)				
Family history of smoking					
Yes	50.82(10.44)	2.10	1.27	0.20	-1.15-5.35
No	48.72(11.15)				
Smoking status					
Smoker	51.52(11.32)	2.40	1.47	0.20	-1.15-5.35
Non-smoker	49.13(10.29)				
Nicotine dependence					
Yes	52.27(12.43)	3.11	1.77	0.08	-0.36 – 6.60
No	49.16(9.9)				

- Fisher's exact test, * - $p<0.05$, SD = standard deviation, CI = Confidence Interval

Table 8 depicts the association between sociodemographic and clinical characteristic with the mean of total PANSS scores.

Male participants were associated with higher total PANSS score and it was statistically significant. Being married, unemployed and with a total personal monthly income of RM500 or less was also associated with higher total PANSS scores, all of which are also statistically significant.

Clinical characteristics with regards to number of hospitalisations, usage of oral antipsychotics were also found to be statistically significant. Participants who has had more than 2 admissions to the psychiatric ward, not on typical oral antipsychotics and taking oral atypical antipsychotics were associated with higher PANSS scores.

Table 12: Multivariate analysis of Total PANSS score among the study participants using multiple linear regression

	Adjusted difference	**p**	**95% CI**
Gender	-2.75	0.09	-5.92 – 0.42
Marital status	4.31	0.01*	1.09 – 7.52
Employment status	3.34	0.07	-0.25 – 6.92
Total income	-1.46	0.49	-5.60 – 2.69
Number of hospitalisations	3.47	0.03*	0.42 – 6.53
Oral typical antipsychotics	0.14	0.96	-5.09 – 5.37
Oral atypical antipsychotics	-3.56	0.17	-8.66 – 1.53

*$p<0.05$

Variables that were found to be statistically significant in univariate analysis were then included into the multivariate analysis of the total PANSS score. As shown in the table above, marital status and the number of hospitalisations were significantly associated with total PANSS scores after adjusting for other possible confounders, namely gender, employment status, total monthly income and the use of either typical or atypical antipsychotics.

4.8 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC FACTORS AND CLINICAL CHARACTERISTICS WITH POSITIVE SYMPTOM SUBSCALE SCORE

Table 13: Association between sociodemographic and clinical characteristics with positive subscale score using t-test

	Mean (SD)	Mean difference	t	P	95% CI
Age					
<40 years old	9.31(2.91)	0.62	1.40	0.16	-0.25-1.49
≥40 years old	8.69(3.01)				
Gender					
Male	9.40(3.31)	1.17	2.57	0.01*	0.27-2.06
Female	8.23(2.08)				
Ethnicity					
Malay	9.33(3.17)	0.64	1.45	0.15	-0.23-1.51
Non-Malay	8.68(2.78)				
Marital status					
Married	8.41(2.41)	-0.82	-1.73	0.09	-1.76-0.12
Not married	9.23(3.17)				
Employment status					
Employed	8.86(2.55)	-0.24	-0.54	0.59	-1.12-0.63
Unemployed	9.11(3.40)				
Total income					
<RM500	8.97(0.27)	-0.03	-0.06	0.95	-1.03-0.97
>RM500	9.00(2.70)				
Education level					
Primary and below	7.92(1.52)	-1.32	-1.97	0.05	-2.47-0.001
Secondary / tertiary	9.15(3.12)				
Drug and alcohol					
Yes	10.52(3.28)	1.75	2.58	0.01*	0.41-3.09
No	8.78(2.88)				
Duration of illness					
12 years or less	9.13(2.82)	0.31	0.70	0.48	-0.56-1.18
More than 12 years	8.82(3.13)				
Number of hospitalisations					
2 or less	7.91(2.08)	-1.73	-3.98	p<0.01*	-2.60- -0.87
More than 2	9.65(3.25)				
Chlorpromazine equivalent (mg)					
≤200 mg/day	8.58(3.02)	-0.84	-1.92	0.06	-1.71-0.03
>200 mg/day	9.42(2.87)				

Typical antipsychotics					
Yes	8.03(1.73)	-1.55	-3.52	p<0.01*	-2.42- -0.68
No	9.58(3.41)				
Atypical antipsychotics					
Yes	9.78(3.29)	1.74	4.09	p<0.01*	0.90-2.58
No	8.04(3.23)				
Anticholinergic					
Yes	9.04(2.69)	0.23	0.45	0.65	-0.77-1.22
No	8.81(3.68)				
Depot antipsychotics					
Yes	8.59(2.96)	-0.62	-1.37	0.17	-1.52-0.28
No	9.21(2.97)				
Benzodiazepines					
Yes	9.38(2.50)	0.46	0.66	0.51	-0.91-1.82
No	8.93(3.03)				
Antidepressants					
Yes	9.44(4.07)	0.49	0.48	0.63	-1.52-2.50
No	8.95(2.92)				
Family history of smoking					
Yes	8.03(1.73)	-1.55	-3.52	p<0.01*	-2.42- -0.68
No	9.58(3.41)				
Smoking status					
Smoker	9.68(3.34)	1.14	2.54	0.01*	0.50-2.40
Non-smoker	8.54(2.64)				
Nicotine dependence					
Yes	10.02(3.36)	1.30	1.43	0.16	-0.52-3.11
No	8.72(3.20)				

* $p < 0.05$

SD= standard deviation, CI = Confidence Interval

Analysis was also done to find association between the sociodemographic and clinical characteristics of the study participants with the positive symptoms scale.

As shown in the table above, several variables were found to be significantly associated with the positive symptoms subscale. Those participants who were male were associated with higher scores on the positive symptom subscale. Those with a history of

drug or alcohol use and with more than 2 hospitalisations to the psychiatric ward were also associated with higher scores.

Lesser positive subscale score were associated with patients taking oral typical antipsychotics whereas scores were higher in those taking atypical antipsychotics. Those with a family history of smoking were associated with lower scores. Smokers also proved to have statistically significant, higher scores on the positive subscale. Although it appeared that nicotine dependence was associated with higher positive subscale scores, this was not statistically significant.

Table 14: Multivariate analysis of PANSS positive symptoms subscale score among the study participants using multivariate linear regression

	Adjusted difference	**p**	**95% CI**
Gender	-0.65	0.21	-1.67 – 0.37
Drug and alcohol	-0.87	0.21	-2.25 – 0.50
Number of hospitalisations	1.46	p<0.01*	0.62 – 2.30
Oral typical antipsychotics	0.16	0.82	-1.27 – 1.60
Oral atypical antipsychotics	-1.37	0.06	-2.78 – 0.02
Family history of smoking	-0.57	0.19	-1.44 – 0.29
Smoking status	0.06	0.91	-1.00 – 1.13

*p<0.05

CI = confidence interval

Univariate analysis found statistically significant association between the following variables with PANSS positive subscale scores: gender, drug and alcohol use, number of hospitalisations, oral typical antipsychotics, oral atypical antipsychotics, family history of smoking and smoking status. Performing multivariate analysis for the variables revealed that only number of hospitalisations was significantly associated with PANSS positive symptom subscale score.

4.9 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS WITH NEGATIVE SYMPTOM SUBSCALE

Table 15: Association between sociodemographic and clinical characteristics with negative symptom subscale score using t-test

	Mean (SD)	Mean difference	t	P	95%CI
Age					
<40 years old	17.95(6.29)	1.06	1.21	0.23	-0.66-2.77
>40 years old	16.90(5.41)				
Gender					
Male	17.30(6.08)	-0.24	-0.26	0.79	-2.03-1.55
Female	65(17.54)				
Ethnicity					
Malay	16.48(5.93)	-1.67	-1.93	0.06	-3.38-0.04
Non-Malay	18.15(5.69)				
Marital status					
Married	15.59(5.12)	-2.60	-2.82	0.01*	-4.42-0.78
Not married	18.19(5.98)				
Employment status					
Employed	16.44(5.08)	-2.02	-2.35	0.02*	-3.717-0.326
Unemployed	18.46(6.46)				
Total income					
<RM500	17.97(5.98)	2.30	2.33	0.02*	0.35-4.24
>RM500	15.67(5.10)				
Education level					
Primary and below	17.92(5.00)	0.63	0.51	0.61	-1.82-3.07
Secondary / tertiary	17.30(5.98)				
Drug and alcohol					
Yes	17.81(4.05)	0.48	0.35	0.73	-2.20-3.16
No	17.33(6.05)				
Duration of illness					
12 years or less	17.27(5.84)	-0.23	-0.27	0.79	-1.95-1.48
More than 12 years	17.51(5.87)				
Number of hospitalisations					
2 or less	16.67(5.89)	-1.17	-1.31	0.53	-2.92-0.59
More than 2	17.84(5.79)				
Chlorpromazine equivalent (mg)					
≤200 mg/day	16.67(5.97)	-1.50	-1.74	0.08	-3.21-0.21
>200 mg/day	18.17(5.63)				
Typical antipsychotics					
Yes	17.29(5.94)	-0.17	-0.18	0.85	-1.93-1.60
No	17.45(5.80)				

Atypical antipsychotics					
Yes	17.83(5.51)	0.96	1.10	0.27	-0.76-2.68
No	16.87(6.20)				
Anticholinergic					
Yes	17.91(5.46)	1.97	2.02	0.04*	0.48-3.90
No	15.94(6.64)				
Depot antipsychotics					
Yes	17.71(6.22)	0.52	0.58	0.56	-1.25-2.29
No	17.19(5.61)				
Benzodiazepines					
Yes	18.10(4.24)	0.801	0.59	0.56	-1.88-3.48
No	17.29(6.02)				
Antidepressants					
Yes	19.56(4.42)	2.28	1.14	0.25	-1.66-6.22
No	17.27(5.89)				
Family history of smoking					
Yes	17.25(5.69)	-0.38	-0.42	0.07	-2.16-1.397
No	17.63				
Smoking status					
Smoker	16.38(6.00)	-1.63	-1.84	0.07	-3.39-0.12
Non-smoker	18.01(5.68)				
Nicotine dependence					
Yes	16.29(6.08)	-0.32	-0.19	0.85	-3.62-2.99
No	16.61(5.92)				

* $p < 0.05$

SD= standard deviation, CI = Confidence Interval

Independent t-test was again performed between sociodemographic and clinical factors and negative symptoms subscale scores of the study participants.

Association was found between marital status, employment status, total personal income and anticholinergic medication use and the PANSS negative symptoms subscale scores. Study participants who were not married had higher mean scores and those working at the time of recruitment were associated with lower mean negative symptoms subscale scores (16.44, SD 5.08). With regards to total monthly personal income, participants who earned RM500 or less in a month were associated with higher scores.

Those who were taking concomitant anticholinergic medication were also associated with higher mean negative symptoms subscale scores.

Table 16: Multivariate analysis of PANSS negative symptoms subscale score among the study participants using multiple linear regression

	B	p	95% CI
Marital status	2.19	0.02*	0.38 - 4.01
Employment status	1.21	0.23	-0.77 - 3.21
Total income	-1.54	0.18	-3.81- 0.73
Anticholinergics	-1.73	0.08	-3.63 – 0.17

*p<0.05

PANSS = Positive and Negative Syndrome Scale, CI= confidence interval

After adjusting for employment status, total income and anticholinergic use, PANSS negative symptoms subscale score was still found to be significantly associated with marital status of the study participants.

4.10 ASSOCIATION BETWEEN SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS WITH GENERAL PSYCHOPATHOLOGY SUBSCALE SCORE

Table 17: Association between sociodemographic and clinical characteristics with general psychopathology subscale score using t-test

	Mean (SD)	Mean difference	t	P	95%CI
Age					
<40 years old	24.00(5.4)	1.46	1.91	0.058	-0.05-2.98
>40 years old	22.54(4.9)				
Gender					
Male	23.92(5.8)	1.97	2.49	0.01*	0.41-3.53
Female	21.95(3.2)				
Ethnicity					
Malay	23.41(5.6)	0.36	0.46	0.64	-1.17-1.89
Non-Malay	23.05(4.7)				
Marital status					
Married	21.64(3.9)	-2.28	-2.79	0.01*	-3.89- -0.66
Not married	23.92(5.5)				
Employment status					
Employed	22.84(4.1)	-0.79	-1.03	0.31	-2.31-0.73
Unemployed	23.64(6.1)				
Total income					
≤RM500	23.41(5.3)	0.76	0.85	0.40	-0.99-2.50
>RM500	22.65(4.6)				
Education level					
Primary and below	22.54(3.5)	-0.79	-0.72	0.47	-2.96-1.38
Secondary / tertiary	23.33(5.4)				
Drug and alcohol					
Yes	25.52(5.2)	2.61	2.20	0.03*	0.26-4.96
No	22.91(5.1)				
Duration of illness					
12 years or less	23.5(4.62)	0.58	0.75	0.45	-0.94-2.10
More than 12 years	22.92(5.7)				
Number of hospitalisations					
2 or less	22.01(5.0)	-1.96	-2.51	0.01*	-3.50- -0.42
More than 2	23.97(5.1)				
Chlorpromazine equivalent (mg)					
≤200 mg/day	22.49(5.6)	-1.52	-1.93	0.04*	-3.03- -0.01
>200 mg/day	24.01(4.5)				
Typical antipsychotics					

Yes	22.29(3.78)	-1.52	-1.93	0.06	-3.06-0.03
No	23.80(5.84)				
Atypical antipsychotics					
Yes	24.37(5.04)	2.51	3.34	p<0.01*	1.03-3.40
No	21.86(5.04)				
Anticholinergic					
Yes	23.89(4.57)	2.53	2.97	p<0.01*	0.85-4.22
No	21.35(6.28)				
Depot antipsychotics					
Yes	22.99(5.99)	-0.37	-0.47	0.64	-1.94-1.20
No	22.36(4.63)				
Benzodiazepines					
Yes	24.24(3.92)	1.16	0.96	0.34	-1.22-3.53
No	23.08(5.32)				
Antidepressants					
Yes	25.22(6.10)	2.11	1.19	0.23	-1.38-5.60
No	23.11(5.13)				
Family history of smoking					
Yes	23.58(5.14)	0.98	1.23	0.22	-0.59-2.55
No	22.60(5.23)				
Smoking status					
Smoker	24.06(6.47)	1.36	1.73	0.09	-0.19-2.92
Non-smoker	22.70(4.14)				
Nicotine dependence					
Yes	24.78(6.57)	2.78	1.59	0.12	-0.72-6.29
No	22.00(5.87)				

* p <0.05

SD= standard deviation, CI = Confidence Interval

The results from the independent t-test performed on the mentioned variables are shown in Table 17.

Males were shown to be associated with higher scores (mean 23.92, SD 5.88) on the general psychopathology subscale. So does being not married, taking drugs and alcohol and being hospitalised more than twice similarly associated. The scores were also higher in those participants taking higher doses of medication (mean chlorpromazine

equivalent dose of more than 200 mg/day), taking oral atypical antipsychotics and on anticholinergic medication.

Table 18: Multivariate analysis of PANSS general psychopathology subscale score among the study participants using multivariate linear regression

	Adjusted difference	p	95% CI
Gender	-1.70	0.06	-3.49 – 0.08
Marital status	1.40	0.08	-0.17 – 2.98
Drug and alcohol	-1.44	0.24	-3.87 – 0.99
Number of hospitalisations	1.36	0.07	-0.13 – 2.85
Cpz equivalent dose	1.02	0.16	-0.42 – 2.45
Oral atypical antipsychotics	-2.21	p<0.01*	-3.65 - - 0.78
Anticholinergics	-1.98	0.02*	-3.61 - - 0.35
Smoking status	0.95	0.31	-0.92 – 2.82

*p<0.05

CI = confidence interval

Use of oral atypical and anticholinergics was still found to be significantly associated with higher general psychopathology subscale scores. This could be an attempt on the clinician's part to control for the symptoms present in the study participants.

4.11 CORRELATION BETWEEN TOTAL PANSS AND ITS SUBSCALE SCORE WITH TOTAL FTND SCORES

Table 19: Correlation between total PANSS, positive symptoms subscale, negative symptoms subscale and general psychopathology subscale scores with total FTND score.

		Total FTND score
Total PANSS	Pearson Correlation	0.07
	p	0.58
Total positive symptoms score	Pearson Correlation	0.13
	p	0.28
Total negative symptoms score	Pearson Correlation	-0.11
	p	0.38
Total general psychopathology score	Pearson Correlation	0.11
	p	0.37

PANSS = Positive and Negative Syndrome Scale

Pearson correlation was used to analyse the correlation between total PANSS scores and each of the subscale scores with total FTND scores. However, the analysis did not reveal any significant correlation.

CHAPTER 5: DISCUSSION

This was a cross sectional study which was initiated to investigate the prevalence of nicotine dependence in an outpatient setting of a state hospital in Negeri Sembilan. It also served to look at other factors associated with nicotine dependence and smoking in a sample of patients with schizophrenia. Objective measures of disease severity were also used to find its association with smoking and nicotine dependence.

5.1 Sociodemographic and clinical characteristics of the study participants

This study was conducted in the outpatient psychiatric clinic of Hospital Tuanku Ja'afar, Seremban. The majority of the study participants were males (64.1%). This is in line with the National Mental Health Registry (NMHR) report which stated that in 2005, 62% of those registered as schizophrenia were males(67).

45.1% of the study participants were Malays, followed by Chinese (38.7%) and Indians (15.5%). This is actually a reflection of the general population in Malaysia, whereby Malays make up the majority. The NMHR report (67) also cited that in 2005, 54% of the registered cases were Malays.

The participants in this study were mostly single(67.4%), which was comparable to the 68% reported by the NMHR. The mean age of the study participants was 41 years old, which was higher than that recorded by the NMHR. Most of the study participants (45.9%) were unemployed. Schizophrenia has been well-recognised as an illness with a high burden of disease and disability, affecting many and more often than not in the reproductive years. Schizophrenia is also generally associated with substantial

impairments in multiple domains of life, including social adjustments and intimacy with others(68).

Unemployment was found to very high in the study participants (45.9%), which is again, comparable to the national numbers(67). Barriers to employment in people with schizophrenia, among others, are clinical factors(69). Frequently cited were active symptoms of schizophrenia and poorer neurocognitive and intrapsychic functioning. 74.6% of the study participants were in the low socioeconomic group, earning less than RM500 per month. This may be in part, due to the fact that the hospital also covers low income communities including those in the rural areas of Negeri Sembilan.

The mean duration of illness of the study participants was 15 years , with a median of 12 years. Most of the patients had been smoking for a mean of 20 years, which means that most of them had started smoking before the onset of illness. Studies have suggested that most patients with schizophrenia who smoked started to do so before the illness itself(70). This suggested that there were vulnerability factors or illness-related factors(71) involved in those who smoke even before the onset of illness or before the emergence of psychotic symptom, as several studies have shown(32, 70).

The mean number of cigarettes smoked in our sample was 17 sticks per day. Most epidemiological studies had defined heavy smoking as smoking more than or equal to 30 sticks per day or 1.5 packs/day(16), which can be considered as a marker of severity of nicotine addiction. Several factors may contribute towards a lower mean amount of cigarettes smoked in our sample. Smoking cessation efforts had received a lot of attention over the years(72). These include the ban on tobacco company-sponsored advertisements and the increase in prices of cigarettes. Smoking cessation campaigns are also an ongoing

effort that the Malaysian government has never stopped putting money into(70). Furthermore, as was discussed earlier, a high number of the study participants are unemployed or earned less than RM500 per month. With the high price of cigarettes, they might not be able to buy them as much as they would like to.

The mean and median dose of medications used by the study participants were lower than those reported in other studies(21, 73). However, these studies were conducted in the inpatient setting, which may have involved patients with more severe illnesses, needing higher dosages of medication to control their symptoms(21) . Our sample also recorded a higher number of participants on oral atypical antipsychotic medications. Over the years, the usage of atypical antipsychotic medication has increased, mostly due to the availability of generic medication, namely Risperidone(74). Admittedly, typical antipsychotics have limited effectiveness and tolerability(75). Therefore, a large proportion of patients were prescribed atypical antipsychotics early on in their treatment. However, studies in this area have to be weighed against the fact that higher doses of typical antipsychotics were used as comparators, thus making it seem that atypical antipsychotics were better tolerated(75).

A high proportion of the study participants had a family history of smoking (63%). A subanalysis of smokers revealed that 78.3% of them had a family history of smoking, strengthening the hypothesis of a familial vulnerability towards smoking and schizophrenia. Freedman et al(76) had described a genetic neurophysiological abnormality in patients with schizophrenia and their relatives. This abnormality was temporarily corrected by high peaks of nicotine.

5.2 Prevalence of smoking and nicotine dependence

The prevalence of smoking obtained in this study was 38.1%. This rate is lower than those found in most studies done in the Western countries. Studies done in the outpatient settings generally appeared to be as high as 88%(13). This rate was almost similar to that found in a study done in Singapore, which found a relatively high prevalence of smoking among Chinese patients with schizophrenia, 31.8% as compared to 16% in the whole Chinese population in Singapore(77). However, this study cannot be generalised to the population in Malaysia as it was conducted only among the Chinese whereas our study had a more diverse ethnic distribution. In Malaysia, the National Mental Health Survey conducted in 1996 estimated that 24.8% of Malaysians smoked(78). Therefore, the rate found in this study is still higher than those in general population in Malaysia. However, more recent numbers are needed to make a more valid comparison.

A meta-analysis study examining association between schizophrenia and tobacco smoking behaviours found a prevalence of 62%(16). However, the meta-analysis included both studies involving in- and outpatient samples. Some reasons can be postulated on why the rate of smoking in our sample was found to be lower. As mentioned before, the Malaysian government had invested a lot in smoking cessation programs. The lower rates of smoking found in our sample of patients may be proof that there is some success to the campaigns amounted by the government. The Malaysia government has also used religious grounds to discourage smoking among the general public.

The prevalence for nicotine dependence found in our study was 73.9%. Nicotine dependence was diagnosed by using the Fagerstrom Test for Nicotine Dependence(FTND), using a cutoff point of 2(61). FTND is the most widely used measure for nicotine dependence. In addition, it has also been found to predict success in stopping smoking(57). In the large National Epidemiological Survey on Alcohol and Related Conditions (NESARC)(24), it was found that nicotine dependence associated with cigarette use constituted 93.7% of all nicotine dependence. However, the survey did not examine the association between nicotine dependence and psychotic disorders. A study done on psychiatric inpatients found that 47.5% of them with the diagnosis of psychotic disorder were nicotine-dependent(29). Our study found a higher percentage. This could be because the other study used a cutoff point of 6 for the FTND. It also studied inpatients and sampled them just before their discharge from the hospital, where access to cigarettes was limited. All this could have artificially lowered the rates found. The mean total FTND score found in our study was 4.16. This was expected as other studies which recorded higher scores were done in Western countries with higher smoking prevalences.

Our study found a smoking cessation rate of 8.8%. However, no data is available regarding smoking cessation rates in the general population in Malaysia. Western studies have quoted low cessation rates when compared with general population(16). Our study did not explore motivation to quit smoking in our sample of participants. However, studies have reported that higher readiness to change or motivation to quit smoking have been associated with success with quitting and more worries with regards to negative

consequences of smoking(79). It was also found that 79% of smokers in an outpatient psychiatric treatment were in the precontemplation stage and were not considering change(80).

5.3 Smoking and nicotine dependence in patients with schizophrenia : associated factors

The finding that being male is associated with smoking is in line with other previous studies done, which also showed a greater preponderance for smoking in men as compared to women(16, 81). Univariate analysis found several other factors to be significantly associated with smoking status in patients with schizophrenia. When controlled for these other (sociodemographic) factors, age, gender, ethnicity and drug and alcohol use was still found to be associated with smoking status. However, this did not replicate the results of other studies which did not show any significant differences between smokers and non-smokers in the sample of patients in terms of demographic variables(28). This could be due to the fact that in Malaysia, the ethnic distribution is more diverse, with the Malays making up the main bulk of it. In studies done in other countries, not much consideration was taken with regards to the ethnicity of their study subjects. In the United States, younger adults who daily had the highest risk of becoming dependent(23). In our sample, those less than 40 years old were found to be more likely to smoke. Efforts should be focused on this age group to reduce the morbidity associated with nicotine dependence. Furthermore, it has also been shown that those who stop smoking before reaching middle age can avoid more than 90% of the mortality associated with lung cancer which is attributed to nicotine(82).

After including all clinical variables found statistically significant in the univariate analysis into the logistics regression analysis, male gender, being Malay, having a total income of more than RM500 and the use and drug and alcohol was still found to be significantly associated with smoking. Due to the high costs of maintaining the smoking habit, it was more likely that our participants had to earn more. Cigarette smoking may be a representation of substance use behaviour with a greater preponderance for the major psychiatric diagnoses(83), thus the finding that the use of drugs and alcohol was significantly associated with smoking.

Other studies have also shown, as in this study, that there were no significant differences between smokers and non-smokers with regards to typical and atypical antipsychotic dosage or in those receiving anticholinergic medication(28). The same study found that patients with schizophrenia who were current smokers were more likely to have been ill longer and had higher number of hospitalisations. This was not found in our study and even though the smokers in our sample appeared to have more hospitalisations, it was not statistically significant. Compared to the study by Patkar et al(28), our study participants were ill for a mean of 14.99 years and hospitalized 1.73 times as opposed to 20.3 years of being ill and hospitalized 6.3 times in the other study. This could explain the difference in the results of the study. However, it was shown with statistical significance that patients who had been ill for more than 12 years scored higher on the FTND.

In terms of nicotine dependence, no significant association was found between the nicotine-dependent and non-dependent smokers with regards to sociodemographic, treatment variables, number of hospitalisations, drug and alcohol use or family history of

smoking. This was also found in another study conducted by Aguilar et al(84). This suggested that nicotine dependence cannot be accounted for by the afore-mentioned factors.

5.4 Smoking and nicotine dependence in patients with schizophrenia : disease severity

PANSS has been commonly used to measure severity of symptoms in patients with schizophrenia. Smoking has been associated with self-medication of symptoms. Various studies done regarding this have found different results. Goff et al(17) found higher levels of positive and negative symptoms via analysis of subscales of the Brief Psychiatric Rating Scale (BPRS). Other studies have also found no difference in PANSS score between smokers and non-smokers(34, 81). Our study found that the total positive and total general psychopathology scores were significantly associated with nicotine dependence. This somewhat supported the hypothesis that patients with positive symptoms self-medicate themselves to reduce these symptoms. This could also explain the higher scores associated with general psychopathology. We found that smokers had lower scores on the negative subscale of PANSS. This was also found in another study done by Ziedonis et al(20). However, it was found to be not significant. The reasons for this could be two-fold : patients are using nicotine to treat their symptoms or nicotine use had modified the clinical presentation by worsening the negative symptoms.

The significance of these two variables were not found in the multivariate analysis. So were univariate analyses done between nicotine dependence and the various

sociodemographic, clinical and other illness-related variables. However, this does not refute the self-medication hypothesis.

5.5 Correlation between nicotine dependence and illness severity

Correlation analysis performed between FTND scores with PANSS total and subscale scores did not reveal any significant association. The study done by Patkar et al(28), however, found significant positive correlations between Fagerstrom scores with PANSS total negative symptom scores but not with the positive symptoms subscale scores. The study done by Patkar et al, however, was conducted in a locked psychiatric inpatient unit which served a predominantly inner-city population. Their sample was composed mostly of patients recently admitted to the hospital. Our study, on the other hand, was done in the outpatient psychiatric unit in a state hospital which serves a heterogenous population. Non-significance can also imply that a bigger study might detect difference between these scores.

CHAPTER 6: LIMITATIONS AND STRENGTHS

The author has identified several limitations of the study:

1. The final sample size of this study did not reach the targeted number, which was calculated as 250 participants. Due to the limited resources available, the researcher did not manage to achieve the targeted sample size. The study involved only a single researcher and the psychiatric outpatient follow-up clinic in Hospital Tuanku Ja'afar, Seremban only ran twice a week. In the future, similar studies would need bigger sample sizes in order to increase the power of the studies. A bigger study would also reduce the chances of a significant finding happening by chance.
2. This study only involved a single site. A multi-centre study would reveal a more generalisable result reflecting the true population of patients with schizophrenia.
3. This was a cross-sectional study, which could only reveal associations between smoking and nicotine dependence with sociodemographic, clinical and other illness-related variables. It cannot suggest cause-effect relationships between the variables.
4. Some of the information obtained from the patients cannot be verified as there was no accompanying guardian. This could, therefore, lead to information bias.
5. Information such as duration of illness may be subject to recall bias. Information the participants' case notes might also not be adequate to confirm the information obtained from the participants.

6. Further measures related to the illness were not taken into account , for example co-morbid anxiety and depression or the presence of extrapyramidal symptoms.
7. Our study did not take into account other variables which might act as confounders to nicotine dependence. Examples of these are the different kings of medication that a patient might be on.

Some identified strengths of the study include :

1. This study can be considered the first study in Malaysia on specifically smoking and nicotine dependence in patients with schizophrenia. It has also opened up new grounds to initiate other studies pertaining to nicotine dependence. Nicotine dependence is a very wide subject which can fuel many more studies in the future. This study can serve as a reference point for future studies in smoking and nicotine dependence in patients with schizophrenia.
2. This study compared patients with schizophrenia who smoked and didn't smoke.
3. The study utilised validated and objective measure including the M.I.N.I and the Fagerstrom Test for Nicotine Dependence (FTND). In this study, most participants had been given the Malay version of FTND, which has also been validated(61).
4. This study was done in the outpatient setting which would constitute a true measure of current smoking. In comparison, inpatient settings would not give a true picture of current smoking behaviour due to the ban on smoking in all the hospitals in Malaysia.

5. The researcher used a handheld device as a way to check for current smoking status. The carbon monoxide monitor can give a general idea of whether the study participants were actual smokers or not.

CHAPTER 7: CONCLUSION AND RECOMMENDATIONS

As a substance which is most commonly used by patients with schizophrenia, its effects on this group of patients need to be recognized as nicotine can also modify the clinical presentation and manifestations of the illness itself. In addition, the increased morbidity and mortality which is associated with nicotine use in patients with schizophrenia cannot be overemphasized.

This study has managed to obtain the objectives which were set out for it. This was a form of pilot study which found a prevalence of 38.1% of smokers in a sample of 181 patients with schizophrenia in an outpatient population in the state hospital of Seremban, Negeri Sembilan. In addition to that, we also found a smoking cessation rate of 8.8%.

Nicotine dependence has been a focus of attention in recent years. Nicotine dependence, diagnosed using the Fagerstrom Test for Nicotine Dependence (FTND) was found in 73.9% of the smokers who completed the FTND.

Smoking was found to be associated with being male, Malay, earning more than RM500 per month and with the use of drugs and alcohol. Nicotine dependence, on the other hand, cannot be explained by sociodemographic factors, clinical characteristics or measures of disease severity which we included in our study. We also did not find any correlation between nicotine dependence and disease severity.

Future studies in the field should attempt to recruit more patients into their study and involve more than one site. It is also recommended to utilize longitudinal study designs that could better establish the cause and effect between nicotine dependence and the many factors that are associated with it. More measures should also be included to

provide objective assessments of illness or medication related issues such as the extrapyramidal symptoms or other tests of cognition.

Other co-morbidities such as depression and anxiety should also be addressed. Higher nicotine dependence have been observed in depressed as compared to non-depressed smokers(24, 85). The association between nicotine dependence and depression and anxiety can also be seen in successful quitters whereby they are less likely to have a lifetime diagnosis of depression and anxiety(86).

It is evident that smoking and nicotine dependence in patients with schizophrenia is fraught with many associated factors which need more exploration . This study had shown that smoking and nicotine dependence are undoubtedly important issues which need to be considered and included into the management of patients with schizophrenia

It can be concluded that nicotine dependence is the most common dual diagnosis in patients with schizophrenia. Withdrawal from nicotine can exacerbate symptoms in patients with schizophrenia. Therefore, smoking cessation programs are important to address issues that may arise and complicate the clinical picture of a patient with schizophrenia.

The focus of smoking cessation in patients with schizophrenia should be on coping skills for negative affect, boredom and handling of situations identified as high risk in addition to education, medication or replacement therapy(87). Instead of addressing motivation to change, an area that needs more attention in smokers with schizophrenia is their low self-efficacy for quitting.

Patients should be made aware and assured of not just the physical and medical benefits of smoking cessation but also of the psychological well-being that they will

experience. Studies have shown that smokers who have stopped for 6 months experienced a decline in psychological problems(88). There were also reports of reduced anxiety levels after quitting, with enduring mood improvements(89) and increased self-esteem(90).

The introduction of smoke-free policies in the mental health settings need co-ordination between inpatient, outpatient and smoking cessation services(91, 92). Specialist services with regards to smokers with mental illness have recorded abstinence rates as high as those in the general population(93). If more active interventions were to be taken in the mental health settings, it is only logical that nicotine dependence should be considered a chronic illness(94).

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APPENDICES

APPENDICES

Appendix A

HELAIAN MAKLUMAT PESAKIT

Sila baca maklumat berikut dengan teliti. Jangan teragak-agak untuk berbincang dengan doktor sekiranya anda mempunyai apa-apa soalan.

Tajuk Kajian

Prevalens, Faktor yang Berkaitan dengan Kebergantungan Nikotin dan Keterukan Penyakit di Kalangan Pesakit Skizofrenia

Pengenalan

Kajian telah menunjukkan kadar merokok yang tinggi di kalangan pesakit psikiatri, sama ada pesakit luar mahupun dalam. Pesakit dengan diagnosa schizophrenia mempunyai kadar merokok yang tinggi (70-80%) sekiranya dibandingkan dengan populasi normal (30-35%) dan semua pesakit psikiatri lain secara amnya (35-54%). Angka ini adalah hampir 3 kali ganda daripada populasi normal dan jauh melebihi kadar yang didapati di kalangan penyakit psikiatri lain.

Merokok dapat dikaitkan dengan dengan pelbagai masalah mental, fizikal dan psikososial. Beberapa model telah dicadangkan untuk menerangkan kadar merokok yang tinggi di kalangan pesakit skizofrenia. Antaranya ialah model perubatan sendiri ("*self-medication model*") yang menyatakan bahawa merokok dapat mengurangkan kesan sampingan ubat antipsikotik dan nikotin boleh memperbaiki gejala negati, kognitif dan/atau kemurungan di kalangan pesakit ini. Penemuan ini mungkin mencerminkan kesan nikotin yang boleh meningkatkan mood, menenangkan dan meningkatkan tahap kesedaran.

Laporan bebrapa kajian juga telah melaporkan bahawa perokok memerlukan dos ubat antipsikotik yang lebih tinggi berbanding mereka yang tidak merokok. Kandungan hidrokarbon polisiklik di dalam asap rokok akan merangsang enzim hati untuk meningkatkan metabolisme ubat antipsikotik.

Kajian yang telah dijalankan mencadangkan bahawa faktor lain seperti masalah keresahan (*anxiety)* dan kemurungan berserta keresahan lebih dikaitkan dengan status merokok daripada masalah kemurungan sahaja. Perokok mengadu lebih banyak masalah keresahan dibandingkan bukan perokok. Merokok dikaitkan dengan peningkatan masalah keresahan dan sekiranya seseorang berhenti merokok, masalah keresahan ini akan berkurang. Beberapa kajian juga telah mendapati bahawa kemurungan meningkatkan kebergantungan terhadap merokok.

Apakah matlamat kajian ini?

Kajian ini bertujuan menilai prevalens dan faktor-faktor yang berkaitan dengan kebergantungan terhadap nikotin serta keterukan penyakit di kalangan pesakit luar dengan skizofrenia di Hospital Tuanku Ja'far, Seremban (HTJS).

Apakah prosedur yang perlu diikuti?

Anda akan diberikan penerangan mengenai kajian ini. Apabila anda telah faham dan bersetuju untuk mengambil bahagian, anda akan diminta agar menandatangani boring keizinan. Kemudian, anda akan ditanya beberapa soalan dan diberi beberapa borang kajiselidik untuk diisi.

Seluruh proses ini akan mengambil masa lebih kurang 30 minit. Selepas itu, anda akan diminta untuk menjalani ujian nafas untuk karbon monoksida.

Kajian ini tidak melibatkan apa-apa intervensi.

Anda digalakkan untuk bertanya soalan sekiranya ada.

Siapa yang tidak boleh menyertai kajian ini?

Mereka yang belum mencapai umur 18 tahun, terlalu sakit ataupun tidak boleh bertutur Bahasa Melayu ataupun Bahasa Inggeris akan dikecualikan daripada menyertai kajian ini.

Apakah manfaat kajian ini:

(a) kepada anda :

Anda akan memberikan kami maklumat yang amat berharga di dalam bidang yang kekurangan data mengenai masalah ini. Ia akan dapat mempengaruhi pengendalian pesakit skizofrenia dengan masalah kebergantungan nikotin.

(b) kepada penyelidik :

Anda akan memberikan kami maklumat yang amat berguna bagi tujuan perancangan untuk persediaan perkhidmatan di masa hadapan.

Apakah kemungkinan kelemahan kajian ini?

Anda perlu menjawab beberapa set borang kajisedlidik yang mungkin mengambil masa lebih kurang 30 minit.

Bolehkah saya menolak daripada menyertai kajian ini?

Boleh. Kajian ini berbentuk sukarela. Sekiranya anda menolak, ia tidak akan mempengaruhi jagaan semasa anda.

Siapakah yang perlu saya hubungi sekiranya saya mempunyai soalan tambahan sepanjang kajian ini dijalankan?

Nama doktor : Dr. Nik Nasyrah Nek Mohd **Tel : 06-7684915**

Appendix B

PATIENT INFORMATION SHEET

Please read the following information carefully, do not hesitate to discuss any questions you may have with your Doctor.

Study Title

Prevalence, Associated Factors of Nicotine Dependence and Disease Severity in Patients with Schizophrenia

Introduction

Numerous studies have consistently demonstrated the high smoking rates among samples of inpatients and outpatient psychiatric patients. Of all the psychiatric diagnoses studied, patients with a diagnosis of schizophrenia have a higher frequency of smoking (70-80%) than the normal population (30 – 35%) and all psychiatric patients in general (35-54%). These rates are nearly 3 times higher than that in the general population and exceeding the rates observed in patients with other psychiatric illnesses.

Smoking has been known to be associated with a number of mental, physical and psychosocial consequences. Several models have been proposed to explain the high rates of smoking in patients with schizophrenia. Among these is the self-medication model that states that smoking reduces the side-effects of antipsychotics and that nicotine can improve the negative, cognitive and/or depressive symptoms in these patients. These findings may reflect the reinforcing properties of nicotine's mood-elevating, calming and alerting effects.

Several studies have also reported that smokers require higher doses of antipsychotics than non-smokers. Polycyclic hydrocarbons in cigarette smoke induces the liver enzymes to increase the metabolism of psychotropic medications.

Previous research have also suggested that other factors such as anxiety and comorbid anxiety and current depression are more highly associated with smoking status than current depression alone. Smokers report more general anxiety than nonsmokers. Smoking is actually associated with increased anxiety and cessation with reduction in anxiety levels. Several studies have also indicated greater degree of dependence in depressed patients.

What is the purpose of this study?

The purpose of this study is to assess the prevalence and associated factors of nicotine dependence and severity of illness in outpatients with schizophrenia in Hospital Tuanku Ja'far, Seremban (HTJS).

What are the procedures to be followed?

You will be given an explanation of the study. Once you have understood and agreed to take part, you will asked to sign a consent form. You will then be asked several questions and given a set of questionnaires to fill out.

It will roughly take 30 minutes to complete the whole process. After that, you will be required to undergo a breath carbon monoxide test.

No intervention will be given.
You are encouraged to ask questions should you have any.

Who should enter this study?

Those who are at least 18 years of age with a diagnosis of schizophrenia will be included in this study.

Who should not enter the study?

Those who are under 18 years of age, too ill (due to an acute medical or mental illness) or who are unable to converse in either English or Malay will be excluded from the study.

What will be benefits of the study:

(a) to you as the subject?

You will be providing us with much needed data in an area of importance. This might have much impact in the future management of patients schizophrenia and nicotine dependence.

(b) to the investigator?
You will be providing us information in an area of management which will be useful in the planning of future services.

What are the possible drawbacks?

A possible drawback is that you will need to answer several sets of

questionnaires which may take up to 30 minutes of your time.

Can I refuse to take part in the study?

Yes, you can. This study is voluntary in nature. It will not have any impact on

your current care should you refuse.

Who should I contact if I have additional questions during the course of the study?

Doctor's Name: Dr. Nik Nasyrah Nek Mohd **Tel: 06-7684915**

Appendix C

CONSENT BY PATIENT FOR CLINICAL RESEARCH

I, ... Identity Card No.....
(Name of Patient)
of.....
(Address)
hereby agree to take part in the clinical research (clinical study/questionnaire study/drug trial) specified below:

Title of Study:
Prevalence, Associated Factors of Nicotine Dependence and Disease Severity in Patients with Schizophrenia
the nature and purpose of which has been explained to me by **Dr. Nik Nasyrah bt Nek Mohamed**
(Name & Designation of Doctor)

and interpreted by .....
(Name & Designation of Interpreter)

..... to the best of his/her ability in ..... language/dialect.

I have been told about the nature of the clinical research in terms of methodology, possible adverse effects and complications (as per patient information sheet). After knowing and understanding all the possible advantages and disadvantages of this clinical research, I voluntarily consent of my own free will to participate in the clinical research specified above.

I understand that I can withdraw from this clinical research at any time without assigning any reason whatsoever and in such a situation shall not be denied the benefits of usual treatment by the attending doctors.

Date: ..... Signature or Thumbprint .....
(Patient)

IN THE PRESENCE OF

Name (.....)

Identity Card No.(.....)

Designation (.....)

Signature
(Witness for Signature of Patient)

I confirm that I have explained to the patient the nature and purpose of the above-mentioned clinical research.

Date .....

Signature
(Attending Doctor)

CONSENT BY RESPONSIBLE RELATIVE FOR CLINICAL RESEARCH

I, ...Identity Card No.....
(Name)
of.....
(Address)

hereby agree that my relative .....I.C. No.....
(Name)
participate in the clinical research (clinical study/questionnaire study/drug trial) specified below:-
Title of Study:
Prevalence, Associated Factors of Nicotine Dependence and Disease Severity in Patients with Schizophrenia
the nature and purpose of which has been explained to me by **Dr. Nik Nasyrah bt Nek Mohamed**
(Name & Designation of Doctor)

and interpreted by .....
(Name & Designation of Interpreter)

..... to the best of his/her ability in ..... language/dialect.

I have been informed of the nature of this clinical research in terms of procedure, possible adverse effects and complications (as per patient information sheet). I understand the possible advantages and disadvantages of participating in this research. I voluntarily give my consent for my relative to participate in this research specified above.

I understand that I can withdraw my relative from this clinical research at any time without assigning any reason whatsoever and in such situation, my relative shall not be denied the benefits of usual treatment by the attending doctors. Should my relative regains his/her ability to consent, he/she will have the right to remain in this research or may choose to withdraw.

Date: ..... Relationship to Patient ..... Signature or Thumbprint .....

IN THE PRESENCE OF

Name (.....)

Identity Card No (.....) .....
Signature
(Witness)

Designation (.....)

I confirm that I have explained to the patient's relative the nature and purpose of the above-mentioned clinical research.

Date ....
Signature
(Attending Doctor)

Appendix D

KEIZINAN OLEH PESAKIT UNTUK PENYELIDIKAN KLINIKAL

Saya,.....No. Kad Pengenalan .....
(Nama Pesakit)

beralamat.....
(Alamat)

dengan ini bersetuju menyertai dalam penyelidikan klinikal (pengajian klinikal/pengajian soal-selidik/percubaan ubat-ubatan) disebut berikut:

TajukPenyelidikan:
Prevalens, Faktor yang Berkaitan dengan Kebergantungan Nikotin dan Keterukan Penyakit di Kalangan Pesakit Skizofrenia
yang mana sifat dan tujuannya telah diterangkan kepada saya oleh **Dr Nik Nasyrah bt Nek Mohamed**
(Nama & Jawatan Doktor)

mengikut terjemahan .....
(Nama & Jawatan Penterjemah)

..... yang telah menterjemahkan kepada saya dengan sepenuh kemampuan dan kebolehannya di dalam Bahasa / loghat.....

Saya telah diberitahu bahawa dasar penyelidikan klinikal dalam keadaan methodologi, risiko dan komplikasi (mengikut kertas maklumat pesakit). Selepas mengetahui dan memahami semua kemungkinan kebaikan dan keburukan penyelidikan klinikal ini, saya merelakan/mengizinkan sendiri menyertai penyelidikan klinikal tersebut di atas.

Saya faham bahawa saya boleh menarik diri dari penyelidikan klinikal ini pada bila-bila masa tanpa memberi sebarang alasan dalam situasi ini dan tidak akan dikecualikan dari kemudahan rawatan dari doktor yang merawat.

Tarikh: .....

.....
Tandatangan/Cap Jari
(Pesakit)

DI HADAPAN

Nama (.....)

No. K/ (.....)

Jawatan (.....)

.....
Tandatangan
(Saksi untuk Tandatangan Pesakit)

Saya sahkan bahawa saya telah menerangkan kepada pesakit sifat dan tujuan penyelidikan klinikal tersebut di atas.

Tarikh: ..... Tandatangan .....
(Doktor yang merawat)

KEIZINAN OLEH WARIS YANG BERTANGGUNGJAWAB UNTUK PENYELIDIKAN KLINIKAL

Saya,..... Kad Pengenalan.....
(Nama Waris yang bertanggungjawab)

beralamat.....
(Alamat)

dengan ini bersetuju supaya saudara saya.....menyertai
(Nama Pesakit)

dalam penyelidikan klinikal (pengajian klinikal/pengajian soal-selidik/percubaan ubat-ubatan) disebut berikut:

TajukPenyelidikan:
Prevalens, Faktor yang Berkaitan dengan Kebergantungan Nikotin dan Keterukan Penyakit di Kalangan Pesakit Skizofrenia
yang mana sifat dan tujuannya telah diterangkan kepada saya oleh **Dr. Nik Nasyrah bt Nek Mohamed**
(Nama & Jawatan Doktor)

.....mengikut terjemahan .....
(Nama & Jawatan Penterjemah)

..... yang telah menterjemahkan kepada saya dengan sepenuh kemampuan dan kebolehannya di dalam Bahasa / loghat.....

Saya telah diberitahu bahawa dasar penyelidikan klinikal dalam keadaan metodologi, risiko dan komplikasi (mengikut kertas maklumat pesakit). Saya mengetahui dan memahami semua kemungkinan kebaikan dan keburukan penyelidikan klinikal ini. Saya merelakan/mengizinkan saudara saya menyertai penyelidikan klinikal tersebut di atas.

Saya faham bahawa saya boleh menarik balik penyertaan saudara saya dalam penyelidikan klinikal ini pada bila-bila masa tanpa memberi sebarang alasan dalam situasi ini dan tidak akan dikecualikan dari kemudahan rawatan dari doktor yang merawat. Sekiranya saudara saya kembali berupaya untuk memberi keizinan, beliau mempunyai hak untuk terus menyertai kajian ini atau memilih untuk menarik diri.

Tarikh: .....

Pertalian dengan Pesakit ....
Tandatangan/Cap Jari Waris
yang bertanggungjawab

DI HADAPAN

Nama (.....)

No. K/P(.....) Tandatangan .....
) *(Saksi untuk Tandatangan*
Jawatan(.....) *Waris yang Bertanggungjawab)*

Saya sahkan bahawa saya telah menerangkan kepada waris yang bertanggungjawab sifat dan tujuan penyelidikan klinikal tersebut di atas.

Tarikh: ..... Tandatangan .....
(Doktor yang merawat)

BK-MIS-1117-E01

Appendix E

Patient Demographic and Clinical Data

Name :

Identification number :

Registration number :

Age :

Gender ☐ Male ☐ Female

Ethnicity ☐ Malay ☐ Chinese ☐ Indian Others _____

Marital status ☐ Single ☐ Married ☐ Divorced

Employment status

☐ Never employed ☐ Self-employed

☐ Employed part-time ☐ Employed full time

☐ Unemployed

Present Occupation

☐ Professional/Technical / Managerial ☐ Service (waiter, maid, barber, security guard)

☐ Agricultural / Fishery / Forestry ☐ Homemaker/Housewife

☐ Military / Police / Fireman ☐ Own business

☐ Factory worker ☐ Student

☐ Clerical / Sales ☐ Others, specify.....

☐ Not employed

Total income earned ☐ <RM500 ☐ RM500-1000

☐ RM1001-2000 ☐ RM 2001-3000

☐ >RM3000

Education level ☐ Primary ☐ Secondary ☐ Nil

☐ College/University ☐ Masters ☐ PhD

Drug and alcohol abuse ☐ No ☐ Yes_____

Duration of illness ☐ Months ☐ Years

Number of hospitalizations ☐

Medication and doses ☐ Typical Dose _____

☐ Atypical Dose_____

☐ Concomitant Dose _____

Breath CO levels _____

Appendix F

M.I.N.I.

MINI INTERNATIONAL NEUROPSYCHIATRIC INTERVIEW

English Version 6.0.0

DSM-IV

USA: D. Sheehan[1], J. Janavs, K. Harnett-Sheehan, M. Sheehan, C. Gray.
[1]University of South Florida College of Medicine- Tampa, USA

EU: Y. Lecrubier[2], E. Weiller, T. Hergueta, C. Allgulander, N. Kadri, D. Baldwin, C. Even.
[2]Centre Hospitalier Sainte-Anne – Paris, France

DISCLAIMER

Our aim is to assist in the assessment and tracking of patients with greater efficiency and accuracy. Before action is taken on any data collected and processed by this program, it should be reviewed and interpreted by a licensed clinician.

This program is not designed or intended to be used in the place of a full medical and psychiatric evaluation by a qualified licensed physician – psychiatrist. It is intended only as a tool to facilitate accurate data collection and processing of symptoms elicited by trained personnel.

M.I.N.I. 6.0.0 (January 1, 2009)

Patient Name:			*Patient Number:*			
Date of Birth:			*Time Interview Began:*			
Interviewer's Name:			*Time Interview Ended:*			
Date of Interview:			*Total Time:*			

	MODULES	TIME FRAME	MEETS CRITERIA	DSM-IV-TR	ICD-10	PRIMARY DIAGNOSIS
A	MAJOR DEPRESSIVE EPISODE	Current (2 weeks)	☐	296.20-296.26 Single	F32.x	☐
		Past	☐	296.20-296.26 Single	F32.x	☐
		Recurrent	☐	296.30-296.36 Recurrent	F33.x	☐
B	SUICIDALITY	Current (Past Month) ☐ Low ☐ Moderate ☐ High	☐			
C	MANIC EPISODE	Current	☐	296.00-296.06	F30.x-F31.9	☐
		Past	☐			
	HYPOMANIC EPISODE	Current	☐	296.80-296.89	F31.8-F31.9/F34.0	☐
		Past	☐			
	BIPOLAR I DISORDER	Current	☐	296.0x-296.6x	F30.x-F31.9	☐
		Past	☐	296.0x-296.6x	F30.x-F31.9	☐
	BIPOLAR II DISORDER	Current	☐	296.89	F31.8	☐
		Past	☐	296.89	F31.8	☐
	BIPOLAR DISORDER NOS	Current	☐	296.80	F31.9	☐
		Past	☐	296.80	F31.9	☐
D	PANIC DISORDER	Current (Past Month)	☐	300.01/300.21	F40.01-F41.0	☐
		Lifetime	☐			
E	AGORAPHOBIA	Current	☐	300.22	F40.00	☐
F	SOCIAL PHOBIA (Social Anxiety Disorder)	Current (Past Month)				
		Generalized	☐	300.23	F40.1	☐
		Non-Generalized	☐	300.23	F40.1	☐
G	OBSESSIVE-COMPULSIVE DISORDER	Current (Past Month)	☐	300.3	F42.8	☐
H	POSTTRAUMATIC STRESS DISORDER	Current (Past Month)	☐	309.81	F43.1	☐
I	ALCOHOL DEPENDENCE	Past 12 Months	☐	303.9	F10.2x	☐
	ALCOHOL ABUSE	Past 12 Months	☐	305.00	F10.1	☐
J	SUBSTANCE DEPENDENCE (Non-alcohol)	Past 12 Months	☐	304.00-.90/305.20-.90	F11.1-F19.1	☐
	SUBSTANCE ABUSE (Non-alcohol)	Past 12 Months	☐	304.00-.90/305.20-.90	F11.1-F19.1	☐
K	PSYCHOTIC DISORDERS	Lifetime	☐	295.10-295.90/297.1/	F20.xx-F29	☐
		Current	☐	297.3/293.81/293.82/ 293.89/298.8/298.9		
	MOOD DISORDER WITH	Lifetime	☐	296.24/296.34/296.44	F32.3/F33.3/	☐
	PSYCHOTIC FEATURES	Current	☐	296.24/296.34/296.44	F30.2/F31.2/F31.5 F31.8/F31.9/F39	☐
L	ANOREXIA NERVOSA	Current (Past 3 Months)	☐	307.1	F50.0	☐
M	BULIMIA NERVOSA	Current (Past 3 Months)	☐	307.51	F50.2	☐
	ANOREXIA NERVOSA, BINGE EATING/PURGING TYPE	Current	☐	307.1	F50.0	☐
N	GENERALIZED ANXIETY DISORDER	Current (Past 6 Months)	☐	300.02	F41.1	☐
O	MEDICAL, ORGANIC, DRUG CAUSE RULED OUT		☐ No	☐ Yes ☐Uncertain		
P	ANTISOCIAL PERSONALITY DISORDER	Lifetime	☐	301.7	F60.2	☐

IDENTIFY THE PRIMARY DIAGNOSIS BY CHECKING THE APPROPRIATE CHECK BOX.
(Which problem troubles you the most or dominates the others or came first in the natural history?)

The translation from DSM-IV-TR to ICD-10 coding is not always exact. For more information on this topic see Schulte-Markwort. Crosswalks ICD-10/DSM-IV-TR. Hogrefe & Huber Publishers 2006.

GENERAL INSTRUCTIONS

The M.I.N.I. was designed as a brief structured interview for the major Axis I psychiatric disorders in DSM-IV and ICD-10. Validation and reliability studies have been done comparing the M.I.N.I. to the SCID-P for DSM-III-R and the CIDI (a structured interview developed by the World Health Organization). The results of these studies show that the M.I.N.I. has similar reliability and validity properties, but can be administered in a much shorter period of time (mean 18.7 ± 11.6 minutes, median 15 minutes) than the above referenced instruments. It can be used by clinicians, after a brief training session. Lay interviewers require more extensive training.

INTERVIEW:

In order to keep the interview as brief as possible, inform the patient that you will conduct a clinical interview that is more structured than usual, with very precise questions about psychological problems which require a yes or no answer.

GENERAL FORMAT:

The M.I.N.I. is divided into modules identified by letters, each corresponding to a diagnostic category.

- At the beginning of each diagnostic module (except for psychotic disorders module), screening question(s) corresponding to the main criteria of the disorder are presented in a gray box.
- At the end of each module, diagnostic box(es) permit the clinician to indicate whether diagnostic criteria are met.

CONVENTIONS:

Sentences written in « normal font » should be read exactly as written to the patient in order to standardize the assessment of diagnostic criteria.

Sentences written in « CAPITALS » should not be read to the patient. They are instructions for the interviewer to assist in the scoring of the diagnostic algorithms.

Sentences written in « **bold** » indicate the time frame being investigated. The interviewer should read them as often as necessary. Only symptoms occurring during the time frame indicated should be considered in scoring the responses.

Answers with an arrow above them (➡) indicate that one of the criteria necessary for the diagnosis(es) is not met. In this case, the interviewer should go to the end of the module, circle « **NO** » in all the diagnostic boxes and move to the next module.

When terms are separated by a *slash (/)* the interviewer should read only those symptoms known to be present in the patient (for example, question G6).

Phrases in (parentheses) are clinical examples of the symptom. These may be read to the patient to clarify the question.

RATING INSTRUCTIONS:

All questions must be rated. The rating is done at the right of each question by circling either Yes or No. Clinical judgment by the rater should be used in coding the responses. Interviewers need to be sensitive to the diversity of cultural beliefs in their administration of questions and rating of responses. The rater should ask for examples when necessary, to ensure accurate coding. The patient should be encouraged to ask for clarification on any question that is not absolutely clear.
The clinician should be sure that each dimension of the question is taken into account by the patient (for example, time frame, frequency, severity, and/or alternatives).
Symptoms better accounted for by an organic cause or by the use of alcohol or drugs should not be coded positive in the M.I.N.I. The M.I.N.I. Plus has questions that investigate these issues.

For any questions, suggestions, need for a training session or information about updates of the M.I.N.I., please contact:
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K. PSYCHOTIC DISORDERS AND MOOD DISORDER WITH PSYCHOTIC FEATURES

ASK FOR AN EXAMPLE OF EACH QUESTION ANSWERED POSITIVELY. CODE YES ONLY IF THE EXAMPLES CLEARLY SHOW A DISTORTION OF THOUGHT OR OF PERCEPTION OR IF THEY ARE NOT CULTURALLY APPROPRIATE. BEFORE CODING, INVESTIGATE WHETHER DELUSIONS QUALIFY AS "BIZARRE".

DELUSIONS ARE "BIZARRE" IF: CLEARLY IMPLAUSIBLE, ABSURD, NOT UNDERSTANDABLE, AND CANNOT DERIVE FROM ORDINARY LIFE EXPERIENCE.
HALLUCINATIONS ARE SCORED "BIZARRE" IF: A VOICE COMMENTS ON THE PERSON'S THOUGHTS OR BEHAVIOR, OR WHEN TWO OR MORE VOICES ARE CONVERSING WITH EACH OTHER.
THE PURPOSE OF THIS MODULE IS TO EXCLUDE PATIENTS WITH PSYCHOTIC DISORDERS. THIS MODULE NEEDS EXPERIENCE.

		Now I am going to ask you about unusual experiences that some people have.			BIZARRE
K1	a	Have you ever believed that people were spying on you, or that someone was plotting against you, or trying to hurt you? NOTE: ASK FOR EXAMPLES TO RULE OUT ACTUAL STALKING.	NO	YES	YES
	b	**IF YES OR YES BIZARRE:** do you currently believe these things?	NO	YES	YES └K6
K2	a	Have you ever believed that someone was reading your mind or could hear your thoughts, or that you could actually read someone's mind or hear what another person was thinking?	NO	YES	YES
	b	**IF YES OR YES BIZARRE:** do you currently believe these things?	NO	YES	YES └K6
K3	a	Have you ever believed that someone or some force outside of yourself put thoughts in your mind that were not your own, or made you act in a way that was not your usual self? Have you ever felt that you were possessed? CLINICIAN: ASK FOR EXAMPLES AND DISCOUNT ANY THAT ARE NOT PSYCHOTIC.	NO	YES	YES
	b	**IF YES OR YES BIZARRE:** do you currently believe these things?	NO	YES	YES └K6
K4	a	Have you ever believed that you were being sent special messages through the TV, radio, newspapers, books or magazines or that a person you did not personally know was particularly interested in you?	NO	YES	YES
	b	**IF YES OR YES BIZARRE:** do you currently believe these things?	NO	YES	YES └K6
K5	a	Have your relatives or friends ever considered any of your beliefs odd or unusual? INTERVIEWER: ASK FOR EXAMPLES. ONLY CODE YES IF THE EXAMPLES ARE CLEARLY DELUSIONAL IDEAS NOT EXPLORED IN QUESTIONS K1 TO K4, FOR EXAMPLE, SOMATIC OR RELIGIOUS DELUSIONS OR DELUSIONS OF GRANDIOSITY, JEALOUSY, GUILT, RUIN OR DESTITUTION, ETC.	NO	YES	YES
	b	**IF YES OR YES BIZARRE:** do they currently consider your beliefs strange?	NO	YES	YES
K6	a	Have you ever heard things other people couldn't hear, such as voices?	NO	YES	
		IF YES TO VOICE HALLUCINATION: Was the voice commenting on your thoughts or behavior or did you hear two or more voices talking to each other?	NO		YES
	b	**IF YES OR YES BIZARRE TO K6a:** have you heard sounds / voices in the past month?	NO	YES	
		IF YES TO VOICE HALLUCINATION: Was the voice commenting on your thoughts or behavior or did you hear two or more voices talking to each other?	NO		YES └K8b

K7 a Have you ever had visions when you were awake or have you ever seen things other people couldn't see? NO YES

CLINICIAN: CHECK TO SEE IF THESE ARE CULTURALLY INAPPROPRIATE.

b IF YES: have you seen these things in the past month? NO YES

CLINICIAN'S JUDGMENT

K8 b IS THE PATIENT CURRENTLY EXHIBITING INCOHERENCE, DISORGANIZED SPEECH, OR MARKED LOOSENING OF ASSOCIATIONS? NO YES

K9 b IS THE PATIENT CURRENTLY EXHIBITING DISORGANIZED OR CATATONIC BEHAVIOR? NO YES

K10 b ARE NEGATIVE SYMPTOMS OF SCHIZOPHRENIA, E.G. SIGNIFICANT AFFECTIVE FLATTENING, POVERTY OF SPEECH (ALOGIA) OR AN INABILITY TO INITIATE OR PERSIST IN GOAL-DIRECTED ACTIVITIES (AVOLITION), PROMINENT DURING THE INTERVIEW? NO YES

K11 a ARE 1 OR MORE « a » QUESTIONS FROM K1a TO K7a CODED YES OR YES BIZARRE AND IS EITHER:

MAJOR DEPRESSIVE EPISODE, (CURRENT, RECURRENT OR PAST)
OR
MANIC OR HYPOMANIC EPISODE, (CURRENT OR PAST) CODED YES? NO YES
└ K13

IF NO TO K11 a, CIRCLE NO IN BOTH 'MOOD DISORDER WITH PSYCHOTIC FEATURES' DIAGNOSTIC BOXES AND MOVE TO K13.

b You told me earlier that you had period(s) when you felt (depressed/high/persistently irritable).

Were the beliefs and experiences you just described (SYMPTOMS CODED YES FROM K1a TO K7a) restricted exclusively to times when you were feeling depressed/high/irritable?

IF THE PATIENT EVER HAD A PERIOD OF AT LEAST 2 WEEKS OF HAVING THESE BELIEFS OR EXPERIENCES (PSYCHOTIC SYMPTOMS) WHEN THEY WERE NOT DEPRESSED/HIGH/IRRITABLE, CODE NO TO THIS DISORDER.

IF THE ANSWER IS NO TO THIS DISORDER, ALSO CIRCLE NO TO K12 AND MOVE TO K13

NO YES

MOOD DISORDER WITH PSYCHOTIC FEATURES

LIFETIME

K12 a ARE 1 OR MORE « b » QUESTIONS FROM K1b TO K7b CODED YES OR YES BIZARRE AND IS EITHER:

MAJOR DEPRESSIVE EPISODE, (CURRENT)
OR
MANIC OR HYPOMANIC EPISODE, (CURRENT) CODED YES?

IF THE ANSWER IS YES TO THIS DISORDER (LIFETIME OR CURRENT), CIRCLE NO TO K13 AND K14 AND MOVE TO THE NEXT MODULE.

NO YES

MOOD DISORDER WITH PSYCHOTIC FEATURES

CURRENT

K13 ARE 1 OR MORE « b » QUESTIONS FROM K1b TO K6b, CODED YES BIZARRE?

OR

ARE 2 OR MORE « b » QUESTIONS FROM K1b TO K10b, CODED YES (RATHER THAN YES BIZARRE)?

AND DID AT LEAST TWO OF THE PSYCHOTIC SYMPTOMS OCCUR DURING THE SAME 1 MONTH PERIOD?

NO YES

PSYCHOTIC DISORDER
CURRENT

K14 IS K13 CODED YES

OR

ARE 1 OR MORE « a » QUESTIONS FROM K1a TO K6a, CODED YES BIZARRE?

OR

ARE 2 OR MORE « a » QUESTIONS FROM K1a TO K7a, CODED YES (RATHER THAN YES BIZARRE)

AND DID AT LEAST TWO OF THE PSYCHOTIC SYMPTOMS OCCUR DURING THE SAME 1 MONTH PERIOD?

NO YES

PSYCHOTIC DISORDER
LIFETIME

Appendix G

PANSS Rating Criteria

Positive Scale (P)

P1 Delusions. Delusions are beliefs that are unfounded, unrealistic, and idiosyncratic. *Basis for rating:* thought content expressed during the interview and its influence on the patient's social relations, and the patient's behavior as reported from primary care workers or family.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	Presence of one or two delusions that are vague, uncrystallized, and not tenaciously held. The delusions do not interfere with the patient's thinking, social relations, or behavior.
4. Moderate	Presence of either a kaleidoscopic array of poorly formed, unstable delusions or a few well-formed delusions that occasionally interfere with the patient's thinking, social relations, or behavior.
5. Moderate severe	Presence of numerous well-formed delusions that are tenaciously held and occasionally interfere with the patient's thinking, social relations, or behavior.
6. Severe	Presence of a stable set of delusions that are crystallized, possibly systematized, tenaciously held, and clearly interfere with the patient's thinking, social relations, and behavior.
7. Extreme	Presence of a stable set of delusions that are either highly systematized or very numerous, and that dominate major facets of the patient's life. This behaviour frequently results in inappropriate and irresponsible action that may even jeopardize the safety of the patient or others.

P2 Conceptual Disorganization. There is a disorganized thinking process characterized by goal-directed sequencing disruptions e.g., circumstantiality, tangentiality, loose associations, non-sequiturs, gross illogicality, or thought block. *Basis for rating:* cognitive-verbal processes observed during the interview.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	The patient's thinking is circumstantial, tangential, or paralogical. He or she has some difficulty directing his or her thoughts toward a goal and some loosening of associations may be evidenced under pressure.
4. Moderate	The patient is able to focus his or her thoughts when communications are brief and structured, but becomes loose or irrelevant when dealing with more complex communications or when under minimal pressure.
5. Moderate severe	The patient generally has difficulty organizing his or her thoughts, as evidenced by frequent irrelevancies, disconnectedness, or loosening of associations even when not under pressure.
6. Severe	The patient's thinking is seriously derailed and internally inconsistent, resulting in gross irrelevancies and disruption of his or her thought processes, which occur almost constantly.
7. Extreme	The patient's thoughts are disrupted to the point where the patient is incoherent. There is marked loosening of associations, which results in total failure of communication (e.g., "word salad" or mutism).

PANSS Rating Criteria

P3 Hallucinatory Behaviour. Verbal report or behavior indicate perceptions that are not generated by external stimuli. These occurrences may be auditory, visual, olfactory, or somatic. *Basis for rating*-verbal report and physical manifestations during the interview as well as behavior reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	One or two clearly formed but infrequent hallucinations, or else a number of vague abnormal perceptions that do not result in thinking or behavior distortions.
4.	Moderate	Hallucinations occur frequently but not continuously, and the patient's thinking and behavior are minimally affected.
5.	Moderate severe	Hallucinations are frequent, may involve more than one sensory modality, and tend to distort thinking and/or disrupt behaviour. The patient may have a delusional interpretation of these experiences and respond to them emotionally and, on occasion, verbally.
6.	Severe	Hallucinations are present almost continuously, causing major thinking and behavior disruptions. The patient treats these experiences as real perceptions, and his or her functioning is impeded by frequent emotional and verbal responses to them.
7.	Extreme	The patient is almost totally preoccupied with hallucinations that virtually dominate his or her thinking and behavior. Hallucinations are rigidly and delusionally interpreted and provoke verbal and behavioral responses, including obedience to command hallucinations.

P4 – Excitement. Hyperactivity is reflected in accelerated motor behavior, heightened responsivity to stimuli, hypervigilance, or excessive mood lability. *Basis for rating:* behavioral manifestations during the interview, as well as behavior reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient tends to be slightly agitated, hyper vigilant, or mildly over aroused throughout the interview, but without distinct episodes of excitement or marked mood lability. The patient's speech may be slightly pressured.
4.	Moderate	Agitation or overarousal is clearly evident throughout the interview, affecting speech and general mobility, or episodic outbursts occur sporadically.
5.	Moderate severe	Significant hyperactivity or frequent outbursts of motor activity are observed, making it difficult for the patient to sit still for longer than several minutes at any given time.
6.	Severe	Marked excitement dominates the interview, delimits attention, and to some extent affects personal functions such as eating and sleeping.
7.	Extreme	Marked excitement seriously interferes with eating and sleeping and makes interpersonal interactions virtually impossible. Acceleration of speech and motor activity may result in the patient's incoherence and exhaustion.

PANSS Rating Criteria

P5 – Grandiosity. There exists an exaggerated self-opinion and unrealistic convictions of superiority, including delusions of extraordinary abilities, wealth, knowledge, fame, power, and moral righteousness. Basis for rating: thought content expressed in the interview and its influence on behavior as reported by primary care workers or family.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	Some expansiveness or boastfulness is evident, but without clear-cut grandiose delusions.
4. Moderate	The patient feels distinctly and unrealistically superior to others. Some poorly formed delusions about special status or abilities may be present but are not acted upon.
5. Moderate severe	Clear-cut delusions concerning remarkable abilities, status, or power are expressed and influence the patient's attitude but not his or her behavior.
6. Severe	Clear-cut delusions of remarkable superiority involving more than one parameter (wealth, knowledge, fame, etc.) are expressed, notably influence interactions, and may be acted upon.
7. Extreme	Thinking, interactions, and behaviour are dominated by multiple delusions of amazing ability, wealth, knowledge, fame, power, and/or moral stature, which may take on a bizarre quality.

P6 – Suspiciousness/Persecution. Unrealistic or exaggerated ideas of persecution are shown, as reflected in guardedness, a distrustful attitude, suspicious hypervigilance, or frank delusions that others mean one harm. *Basis of rating:* thought content expressed in the interview and its influence on behavior as reported by primary care workers or family.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	The patient presents a guarded or even openly distrustful attitude, but his or her thoughts, interactions, and behavior are minimally affected.
4. Moderate	The patient's distrustfulness is clearly evident and intrudes on the interview and/ or his or her behaviour, but there is no evidence of persecutory delusions. Alternatively, there may be indications of loosely formed persecutory delusions, but these do not seem to affect the patient's attitude or interpersonal relations.
5. Moderate severe	The patient shows marked distrustfulness, leading to major disruptions in his or her interpersonal relations, or else there are clear-cut persecutory delusions that have limited impact on his or her interpersonal relations and behaviour.
6. Severe	Clear-cut pervasive delusions of persecution that may be systematized significantly interfere in the patient's interpersonal relations.
7. Extreme	A network of systematized persecutory delusions dominates the patient's thinking, social relations, and behavior.

PANSS Rating Criteria

P7 – Hostility. There are verbal and nonverbal expressions of ange sarcasm, passive-aggressive behavior, verbal abuse, and assaultiv interpersonal behavior observed during the interview and reports by family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient shows indirect or restrained communication of anger, such as sarcasm, disrespect, hostile expressions, and occasional irritability.
4.	Moderate	The patient presents an overtly hostile attitude, showing frequent irritability and direct expression of anger or resentment.
5.	Moderate severe	The patient is highly irritable and occasionally verbally abusive or threatening.
6.	Severe	Uncooperativeness and verbal abuse or threats notably influence the interview and seriously impact upon the patient's social relations. The patient may be violent and destructive but is not physically assaultive toward others.
7.	Extreme	Marked anger by the patient results in extreme uncooperativeness, precluding other interactions, or in a physical assault episode directed toward others.

PANSS Rating Criteria

Negative Scale (N)

N1 – Blunted Affect. There is diminished emotional responsiveness characterized by a reduction in facial expression, modulation of feelings, and communicative gestures. *Basis for rating:* observation of the patient's affective tone and emotional responsiveness during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	Changes in the patient's facial expression and communicative gestures seem to be stilted, forced, artificial, or lacking in modulation.
4.	Moderate	The patient displays a reduced range of facial expression and few expressive gestures, resulting in a dull appearance.
5.	Moderate severe	Affect is generally "flat," with only occasional changes in the patient's facial expression and few communicative gestures.
6.	Severe	The patient exhibits marked flatness and a deficiency of emotions most of the time. There may be unmodulated extreme affective discharges, such as excitement, rage, or inappropriate uncontrolled laughter.
7.	Extreme	Changes in the patient's facial expression and evidence of communicative gestures are virtually absent. The patient seems constantly to show a barren or "wooden" expression.

N2 – Emotional Withdrawal. There is a lack of interest in, involvement with, and affective commitment to life events. *Basis for rating:* reports of functioning from primary care workers or family, and interpersonal behavior observations during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient usually lacks initiative and may occasionally show deficient interest in surrounding events.
4.	Moderate	The patient is generally emotionally distanced from his or her surroundings and its challenges but can be engaged with encouragement.
5.	Moderate severe	The patient is clearly emotionally detached from other people and his or her surroundings, resisting all efforts at engagement. The patient appears distant, docile, and purposeless, but can be involved in communication at least briefly and tends to his or her personal needs, sometimes with assistance.
6.	Severe	The patient's marked deficiency of interest and emotional commitment results in limited conversation with others and frequent neglect of personal functions, for which the patient requires supervision.
7.	Extreme	The patient is almost totally withdrawn, uncommunicative, and neglectful of his or her personal needs, resulting from a profound lack of interest and emotional commitment.

PANSS Rating Criteria

N3 – Poor Rapport. There is a lack of interpersonal empathy, a lack of openness in conversation, and also a minimal sense of closeness, interest or involvement with the interviewer. Poor rapport is evidenced by interpersonal distancing and reduced verbal and nonverbal communication. *Basis for rating:* interpersonal behavior during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient's conversation is characterized by a stilted, strained, or artificial tone. It may lack emotional depth or tend to remain on an impersonal, intellectual plane.
4.	Moderate	The patient is typically aloof, with interpersonal distancing evident in his or her behavior. The patient may answer questions mechanically, act bored, or express disinterest.
5.	Moderate severe	The patient's disinvolvement is obvious and clearly impedes interview's productivity. The patient may tend to avoid eye or face contact.
6.	Severe	The patient is highly indifferent, with marked interpersonal distance. His or her answers are perfunctory, and there is little nonverbal evidence of involvement. The patient frequently avoids eye and face contact.
7.	Extreme	The patient is totally uninvolved with the interviewer. He or she appears to be completely indifferent and consistently avoids verbal and nonverbal interactions during the interview.

N4 – Passive/Apathetic Social Withdrawal. Diminished interest and initiative in social interactions due to passivity, apathy, anergy, or avolition leading to reduced interpersonal involvements and neglect of daily living activities. *Basis for rating:* social behavior reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patients shows occasional interest in social activities but poor initiative. He or she usually engages others only when first approached by them.
4.	Moderate	The patient passively goes along with most social activities but in a disinterested or mechanical way. He or she tends to recede into the background.
5.	Moderate severe	The patient passively participates in few activities and shows virtually no interest or initiative. Generally, he or she spends little time with others.
6.	Severe	The patient tends to be apathetic and isolated, participating very rarely in social activities and occasionally neglecting his or her personal needs. The patient has very few spontaneous social contacts.
7.	Extreme	The patient is profoundly apathetic, socially isolated, and personally neglectful.

PANSS Rating Criteria

N5 – Difficulty in Abstract Thinking. The patient shows impairment using the abstract-symbolic thinking mode, as demonstrated by difficulty with classification, forming generalizations, and moving beyond concrete or egocentric thinking in problem-solving tasks. *Basis for rating:* responses to questions on similarities and proverb interpretation, and use of concrete vs. abstract mode during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient tends to give literal or personalized interpretations to the more difficult proverbs and may have some problems with concepts that are fairly abstract or remotely related.
4.	Moderate	The patient often utilizes a concrete mode. He or she has difficulty with most proverbs and some categories and tends to be distracted by functional aspects and salient features.
5.	Moderate severe	The patient deals primarily in a concrete mode, exhibiting difficulty with most proverbs and many categories.
6.	Severe	The patient is unable to grasp the abstract meaning of proverbs or figurative expressions and can formulate classifications for only the most simple of similarities. The patient's thinking is either vacuous or locked into functional aspects, salient features, and idiosyncratic interpretations.
7.	Extreme	The patient can only use concrete thinking modes. He or she shows no comprehension of proverbs, common metaphors or similes, and simple categories. Even salient and functional attributes do not serve as a basis for classification. This rating may apply to those who cannot interact even minimally with the examiner due to marked cognitive impairment.

N6 – Lack of Spontaneity and Flow of Conversation. There is a reduction in the normal flow of communication associated with apathy, avolition, defensiveness, or cognitive deficit. This disruption in normal flow is manifested by diminished fluidity and productivity of the verbal-interactional process. *Basis for rating:* cognitive-verbal processes observed during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	There is little initiative in the patient's conversation. The patient's answers tend to be brief and unembellished, requiring direct and leading questions by the interviewer.
4.	Moderate	The patient's conversation lacks free flow and appears uneven or halting. Leading questions are frequently needed to elicit adequate responses and proceed with the conversation.
5.	Moderate severe	The patient shows a marked lack of spontaneity and openness, replying to the interviewer's questions with only one or two brief sentences.
6.	Severe	The patient's responses are limited mainly to a few words or short phrases intended to avoid or curtail communication (e.g., "I don't know" or "I'm not at liberty to say"). The conversation is seriously impaired as a result, and the interview is highly unproductive.
7.	Extreme	The patient's verbal output is restricted to an occasional utterance at most, making conversation impossible.

PANSS Rating Criteria

N7 – Stereotyped Thinking. There is decreased fluidity, spontaneity, and flexibility of thinking, as evidenced in rigid, repetitious, or barren thought content. *Basis for rating:* cognitive-verbal processes observed during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	There is some rigidity in the patient's attitudes or beliefs. The patient may refuse to consider alternative positions or have difficulty shifting from one idea to another.
4.	Moderate	Conversation with the patient revolves around a recurrent theme, resulting in difficulty shifting to a new topic.
5.	Moderate severe	The patient's thinking is so rigid and repetitious that, despite the interviewer's efforts, conversation is limited to only two or three dominating topics.
6.	Severe	The patient's uncontrolled repetition of demands, statements, ideas, or questions severely impairs conversation.
7.	Extreme	The patient's thinking, behaviour, and conversation are dominated by constant repetition of fixed ideas or limited phrases, leading to gross rigidity, inappropriateness, and restrictive communication.

PANSS Rating Criteria

General Psychopathology Scale (G)

G1 – Somatic Concern. There are physical complaints or beliefs about bodily illness or malfunctions. The patient's concerns may range from a vague sense of ill-being to clear-cut delusions of catastrophic physical disease. *Basis for rating:* thought content expressed in the interview.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	The patient has a concern about health or somatic issues demonstrated by occasional questions and a desire for reassurance.
4. Moderate	The patient complains about poor health or bodily malfunction, but there is no delusional conviction and over-concern can be allayed by reassurance.
5. Moderate severe	The patient expresses numerous or frequent complaints about physical illness or bodily malfunction or else the patient reveals one or two clear-cut delusions involving these themes but is not preoccupied by them.
6. Severe	The patient is preoccupied by one or a few clear-cut delusions about physical disease or organic malfunction, but the patient's affect is not fully immersed in these themes, and his or her thoughts can be diverted by the interviewer with some effort.
7. Extreme	The patient experiences numerous and frequently reported somatic delusions, or only a few somatic delusions of a catastrophic nature, which totally dominate his or her affect and thinking.

G2 – Anxiety. There are subjective experiences of nervousness, worry, apprehension, or restlessness, ranging from excessive concern about the present or future to feelings of panic. *Basis for rating:* verbal report during the interview and corresponding physical manifestations.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	The patient expresses some worry, over-concern, or subjective restlessness, but no somatic and behavioral consequences are reported or evident.
4. Moderate	The patient reports distinct nervousness symptoms, which are reflected in mild physical manifestations such as fine hand tremors and excessive perspiration.
5. Moderate severe	The patient reports serious anxiety problems that have significant physical and behavioral consequences such as marked tension, poor concentration, palpitations, or impaired sleep.
6. Severe	The patient has a subjective state of almost constant fear associated with phobias, marked restlessness, or numerous somatic manifestations.
7. Extreme	The patient's life is seriously disrupted by anxiety, which is present almost constantly and, at times, reaches panic proportion or is manifested in actual panic attacks.

PANSS Rating Criteria

G3 – Guilt Feelings. The patient exhibits a sense of remorse or self-blame for real or imagined misdeeds in the past. *Basis for rating:* verbal report of guilt feelings during the interview and the influence of these feelings on the patient's attitudes and thoughts.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	Questioning the patient elicits a vague sense of guilt or self-blame for a minor incident, but he or she is clearly not overly concerned.
4.	Moderate	The patient expresses distinct concern over his or her responsibility for a real incident in his or her life but is not preoccupied with it and his or her attitude and behavior are essentially unaffected.
5.	Moderate severe	The patient expresses a strong sense of guilt associated with self-deprecation or the belief that he or she deserves punishment. The guilt feelings may have a delusional basis, may be volunteered spontaneously, may be a source of preoccupation and/or depressed mood, and cannot be allayed readily by the interviewer.
6.	Severe	The patient has strong ideas of guilt that take on a delusional quality and lead to an attitude of hopelessness or worthlessness. The patient believes he or she should receive harsh sanctions for the misdeeds and may even regard his or her current life situation as such punishment.
7.	Extreme	The patient's life is dominated by unstable delusions of guilt, for which he or she feels deserving of drastic punishment, such as life imprisonment, torture, or death. There may be associated suicidal thoughts or attribution of others' problems to his or her own past misdeeds.

G4 – Tension. There are overt physical manifestations of fear, anxiety, and agitation, such as stiffness, tremors, profuse sweating, and restlessness. *Basis for rating:* verbal report attesting to anxiety and, thereupon, the severity of physical manifestations of tension observed during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient's posture and movements indicate slight apprehension, such as minor rigidity, occasional restlessness, position shifting, or fine rapid hand tremors.
4.	Moderate	A clearly nervous appearance emerges from various manifestations, such as fidgety behavior, obvious hand tremor, excessive perspiration, or nervous mannerisms.
5.	Moderate severe	The patient displays pronounced tension through numerous manifestations, such as nervous shaking, profuse sweating, and restlessness, but his or her interview conduct is not significantly affected.
6.	Severe	The patient displays pronounced tension that disrupts interpersonal interactions. The patient, for example, may be constantly fidgeting, may be unable to sit still for long, or may hyperventilate.
7.	Extreme	The patient's marked tension is manifested by signs of panic or gross motor acceleration, such as rapid restless pacing and the inability to remain seated for longer than a minute, which makes sustained conversation impossible.

PANSS Rating Criteria

G5 – Mannerisms and Posturing. Unnatural movements or posture are shown as characterized by an awkward, stilted, disorganized, or bizarre appearance. *Basis for rating:* observation of physical manifestations during the interview as well as reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	Slight awkwardness in the patient's movements or minor posture rigidity .
4.	Moderate	The patient's movements are notably awkward or disjointed, or an unnatural posture is maintained for brief periods.
5.	Moderate severe	The patient displays occasional bizarre rituals or a contorted posture or the patient sustains an abnormal position for extended periods.
6.	Severe	The patient frequently repeats bizarre rituals, mannerisms, or stereotyped movements, or the patient sustains a contorted posture for extended periods.
7.	Extreme	The patient's functioning is seriously impaired by virtually constant involvement in ritualistic, manneristic, or stereotyped movements or by an unnatural fixed posture sustained most of the time.

G6 – Depression. There are feelings of sadness, discouragement, helplessness, and pessimism. *Basis for rating:* verbal report of depressed mood during the interview and its observed influence on the patient's attitude and behavior as reported from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient expresses some sadness or discouragement when questioned, but there is no evidence of depression in the patient's general attitude or demeanor.
4.	Moderate	The patient has distinct feelings of sadness or hopelessness, which may be spontaneously divulged, but his or her depressed mood has no major impact on his or her behavior or social functioning, and he or she can usually be cheered up.
5.	Moderate severe	The patient's mood is distinctly depressed and associated with obvious sadness, pessimism, loss of social interest, psychomotor retardation, and some interference in his or her appetite and sleep. The patient cannot be easily cheered up.
6.	Severe	The patient's markedly depressed mood is associated with sustained feelings of misery, hopelessness, worthlessness, and occasional crying. There is also major interference with his or her appetite and/or sleep as well as normal motor and social functions, possibly with signs of self-neglect.
7.	Extreme	Depressive feelings seriously interfere with most major functions. These manifestations include frequent crying, pronounced somatic symptoms, impaired concentration, psychomotor retardation, social disinterest, self-neglect, possible depressive or nihilistic delusions, and/or possible suicidal thoughts or actions.

PANSS Rating Criteria

G7 – Motor Retardation. There is a reduction in motor activity reflected by the slowing or lessening of movements and speech, diminished responsiveness to stimuli, and reduced body tone. *Basis for rating:* manifestations during the interview as well as reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	Slight, but noticeable diminution in the patient's movements and speech rate. The patient may be somewhat underproductive in conversation and gestures.
4.	Moderate	The patient clearly has slow movements, and his or her speech may be characterized by poor productivity, including long response latency, extended pauses, or a slow pace.
5.	Moderate severe	A marked reduction in the patient's motor activity renders communication highly unproductive or delimits functioning in social and occupational situations. The patient can usually be found sitting or lying down.
6.	Severe	The patient's movements are extremely slow, resulting in minimal activity and speech. Essentially, the patient's day is spent sitting idly or lying down.
7.	Extreme	The patient is almost completely immobile and virtually unresponsive to external stimuli.

G8 – Uncooperativeness. There is an active refusal to comply with the will of significant others, including the interviewer, hospital staff, or family, perhaps associated with distrust, defensiveness, stubbornness, negativism, rejection of authority, hostility, or belligerence. *Basis for rating:* interpersonal behavior observed during the interview as well as reports from care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient complies to requests with resentment, impatience, or sarcasm. He or she may inoffensively object to sensitive probing during the interview.
4.	Moderate	The patient occasionally refuses outright to comply with normal social demands, such as making his or her own bed, attending scheduled programs, etc. The patient may project a hostile, defensive, or negative attitude but usually it is possible to work with him or her.
5.	Moderate severe	The patient is frequently incompliant with the demands of his or her surroundings and may be characterized by others as an "outcast" or as having "serious attitude problems." His or her uncooperativeness is reflected in obvious defensiveness or irritability with the interviewer and possible unwillingness to address many questions.
6.	Severe	The patient is highly uncooperative, negativistic, and possibly belligerent. He or she refuses to comply with most social demands and may be unwilling to initiate or conclude the full interview.
7.	Extreme	The patient's active resistance to others seriously impacts on virtually all major areas of his or her functioning. The patient may refuse to join any social activities, tend to personal hygiene, converse with family or staff, or participate even briefly in interviews.

PANSS Rating Criteria

G9 – Unusual Thought Content. Thinking is characterized by strange, fantastic, or bizarre ideas, ranging from those that are remote or atypical to those that are distorted, illogical, and patently absurd. *Basis for rating:* thought content expressed during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient's expressed thought content is somewhat peculiar or idiosyncratic, or familiar ideas are framed in an odd context.
4.	Moderate	The patient's ideas are frequently distorted and occasionally seem quite bizarre.
5.	Moderate severe	The patient expresses many strange and fantastic thoughts (e.g., being the adopted child of a king, being an escapee from death row) or some that are patently absurd (e.g., having hundreds of children, receiving radio messages from outer space through a tooth filling).
6.	Severe	The patient expresses many illogical or absurd ideas or some that have a distinctly bizarre quality (e.g., having three heads, being a visitor from another planet).
7.	Extreme	The patient's thinking is replete with absurd, bizarre, and grotesque ideas.

G10 – Disorientation. There is a lack of awareness of one's relationship to one's surroundings, including persons, place, and time that may be due to confusion or withdrawal. *Basis for rating:* responses to interview questions on orientation.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient's general orientation is adequate but he or she has some difficulty with specifics. For example, patient knows his or her location but not the street address; hospital staff names but not their functions; the month but confuses the day of week with an adjacent day; or mistakes the date by more than two days. He or she may have narrow interests demonstrated by familiarity with his or her immediate, but not extended, surroundings (e.g., the ability to identify staff but not the mayor, governor, or president).
4.	Moderate	There is only partial success recognizing persons, places, and time. For example, the patient knows he or she is in a hospital but not its name; the name of his or her city but not the borough or district; the name of his or her primary therapist but not those of other direct care workers; or the year and season but is unsure of the month.
5.	Moderate severe	There is considerable failure recognizing persons, places, and time. The patient has only a vague notion of where he or she is and seems unfamiliar with most people in his or her surroundings. He or she may identify the year correctly or nearly so but not know the current month, day of week, or even the season.
6.	Severe	There is marked failure recognizing persons, places, and time. For example, the patient has no knowledge of his or her whereabouts, confuses the date by more than one year, or can only name one or two individuals in his or her current life.
7.	Extreme	The patient appears completely disoriented with regard to persons, places, and time. There is severe confusion or total ignorance about his or her location, the current year, and even the most familiar people, such as his or her parents, spouse, friends, and primary therapist.

PANSS Rating Criteria

G11 - Poor Attention. Poor focused alertness is manifested by poor concentration, distractibility from internal and external stimuli, and difficulty in harnessing, sustaining, or shifting focus to new stimuli. *Basis for rating:* manifestations during the interview.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	The patient has limited concentration demonstrated by occasional vulnerability to distraction or his or her faltering attention toward the end of the interview.
4. Moderate	The patient's conversation is affected by the tendency to be easily distracted, difficulty in sustaining concentration on a given topic, or problems with shifting attention to new topics.
5. Moderate severe	The patient's conversation is seriously hampered by poor concentration, distractibility, and difficulty with appropriately shifting his or her focus.
6. Severe	The patient's attention can be harnessed for only brief moments or with great effort, due to marked distraction by internal or external stimuli.
7. Extreme	The patient's attention is so disrupted that even brief conversation is impossible.

G12 – Lack of Judgement and Insight. There is an impaired awareness or understanding of one's own psychiatric condition and life situation. This impairment is evidenced by the patient's inability to recognize past or present psychiatric illness or symptoms, denial of his or her need for psychiatric hospitalization or treatment, decisions characterized by poor anticipation of the consequences, and unrealistic short-term and long-range planning. *Basis of rating:* thought content expressed during the interview.

1. Absent	The definition does not apply.
2. Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3. Mild	The patient recognizes having a psychiatric disorder but clearly underestimates its seriousness, the implications for treatment, or the importance of taking measures to avoid relapse. His or her future planning may be poorly conceived.
4. Moderate	The patient shows a vague or shallow recognition of his or her illness. There may be fluctuations in his or her acknowledgement of being ill or little awareness of the major symptoms that are present, such as delusions, disorganized thinking, suspiciousness, and social withdrawal. The patient may rationalize the need for treatment as a way of relieving lesser symptoms, such as anxiety, tension, and sleep difficulty.
5. Moderate severe	The patient acknowledges the past but not the present psychiatric disorder. If challenged, he or she may concede to the presence of some unrelated or insignificant symptoms that tend to be explained away with severe misinterpretation or delusional thinking. His or her need for psychiatric treatment similarly goes unrecognized.
6. Severe	The patient denies ever having a psychiatric disorder. He or she disavows the presence of any psychiatric symptoms in the past or present and, though compliant, denies the need for treatment and hospitalization.
7. Extreme	The patient emphatically denies his or her past and present psychiatric illness. Current hospitalization and treatment are given a delusional interpretation (e.g., as punishment for misdeeds, as persecution by tormentors, etc.), and the patient may thus refuse to cooperate with therapists, medication, or other aspects of treatment.

PANSS Rating Criteria

G13 – Disturbance of volition. There is disturbance in the wilful initiation, sustenance, and control of one's thoughts, behavior, movements, and speech. *Basis for rating:* thought content and behavior manifested during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	There is some evidence of indecisiveness in the patient's conversation and thinking that may impede his or her verbal and cognitive processes to a minor extent.
4.	Moderate	The patient is often ambivalent and shows clear difficulty reaching decisions. His or her conversation may be marred by thinking alternation, and consequently, his or her verbal and cognitive functioning are clearly impaired.
5.	Moderate severe	Disturbance of volition interferes with the patient's thinking and behavior. The patient shows pronounced indecision that impedes the initiation and continuation of social and motor activities, and which may also be evidenced in halting speech.
6.	Severe	Disturbance of volition interferes in the execution of simple, automatic motor functions, such as dressing and grooming, and markedly affects the patient's speech.
7.	Extreme	The patient's almost complete failure of volition is manifested by severe inhibition of his or her movement and speech, resulting in immobility and/or mutism.

G14 - Poor Impulse Control. There is disordered regulation and control when acting on inner urges, resulting in sudden, unmodulated, arbitrary, or misdirected discharge of tension and emotions without concern about the consequences. *Basis for rating:* the patient's behavior during the interview and reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient tends to be easily angered and frustrated when facing stress or denied gratification but rarely acts on impulse.
4.	Moderate	The patient gets angered and verbally abusive with minimal provocation. He or she may be occasionally threatening, destructive, or have one or two episodes involving physical confrontation or a minor brawl.
5.	Moderate severe	The patient exhibits repeated impulsive episodes involving verbal abuse, destruction of property, or physical threats. There may be one or two episodes involving serious assault, for which the patient requires isolation, physical restraint, or p.r.n. sedation.
6.	Severe	The patient is frequently impulsively aggressive, threatening, demanding, and destructive, without any apparent consideration of the consequences. He or she shows assaultive behavior, may also be sexually offensive, and possibly responds behaviourally to hallucinatory commands.
7.	Extreme	The patient exhibits homicidal attacks, sexual assaults, repeated brutality, or self-destructive behavior. He or she requires constant direct supervision or external constraints because of his or her inability to control dangerous impulses.

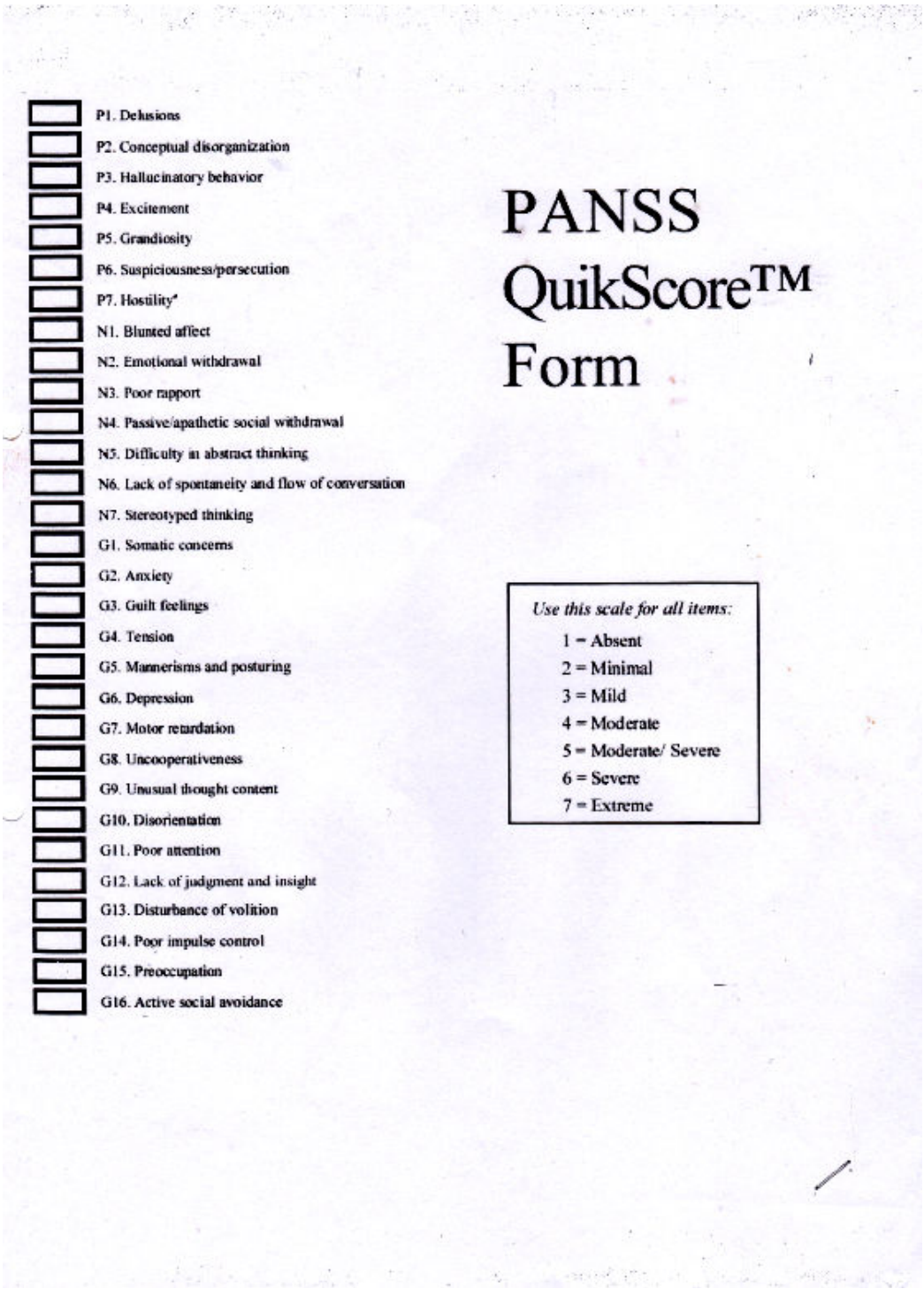
PANSS Rating Criteria

G15 – Preoccupation. There is absorption with internally generated thoughts and feelings or with autistic experiences to the detriment of reality orientation and adaptive behavior. *Basis for rating:* interpersonal behavior observed during the interview.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	Excessive involvement in personal needs or problems, such that the patient's conversation veers back to egocentric themes and his or her concern for others is diminished.
4.	Moderate	The patient occasionally appears self-absorbed, as if daydreaming or involved with internal experiences that interfere with communication to a minor extent.
5.	Moderate severe	The patient often appears engaged in autistic experiences, as evidenced by behaviors that significantly intrude on social and communicational functions, such as staring vacantly , muttering or talking to himself or herself, or involvement with stereotyped motor patterns.
6.	Severe	The patient displays marked preoccupation with autistic experiences that seriously delimits his or her concentration, ability to converse, and orientation to the surroundings. The patient may frequently smile, laugh, mutter, talk, or shout to himself or herself.
7.	Extreme	The patient is severely absorbed with autistic experiences that profoundly affect all major realms of the patient's behavior. He or she may constantly respond verbally and behaviorally to hallucinations and show little awareness of other people or the external surroundings.

G16- Active Social Avoidance. There is diminished social involvement associated with unwarranted fear, hostility, or distrust. *Basis for rating:* social functioning reports from primary care workers or family.

1.	Absent	The definition does not apply.
2.	Minimal	Questionable pathology; the patient may be at the upper extreme of normal limits.
3.	Mild	The patient seems ill at ease with others and prefers to spend time alone, although he or she participates in social functions when required.
4.	Moderate	The patient grudgingly attends all or most social activities but may leave prematurely on account of anxiety, suspiciousness, or hostility.
5.	Moderate severe	The patient fearfully or angrily keeps away from many social interactions despite others' efforts to engage him or her and tends to spend unstructured time alone.
6.	Severe	The patient participates in very few social activities because of his or her fear, hostility, or distrust. When approached, the patient shows a strong tendency to break off interactions, and generally he or she appears to isolate himself or herself from others.
7.	Extreme	The patient cannot be engaged in social activities because of pronounced fears, hostility, or persecutory delusions. He or she avoids all interactions and remains isolated from others as much as possible.


P1. Delusions
P2. Conceptual disorganization
P3. Hallucinatory behavior
P4. Excitement
P5. Grandiosity
P6. Suspiciousness/persecution
P7. Hostility*
N1. Blunted affect
N2. Emotional withdrawal
N3. Poor rapport
N4. Passive/apathetic social withdrawal
N5. Difficulty in abstract thinking
N6. Lack of spontaneity and flow of conversation
N7. Stereotyped thinking
G1. Somatic concerns
G2. Anxiety
G3. Guilt feelings
G4. Tension
G5. Mannerisms and posturing
G6. Depression
G7. Motor retardation
G8. Uncooperativeness
G9. Unusual thought content
G10. Disorientation
G11. Poor attention
G12. Lack of judgment and insight
G13. Disturbance of volition
G14. Poor impulse control
G15. Preoccupation
G16. Active social avoidance
PANSS
QuikScore™
Form
Use this scale for all items:
1 = Absent
2 = Minimal
3 = Mild
4 = Moderate
5 = Moderate/ Severe
6 = Severe
7 = Extreme

Appendix H

Fagerstrom Test for Nicotine Dependence *

Is smoking "just a habit" or are you addicted? Take this test and find out your level of dependence on nicotine.

1. How soon after you wake up do you smoke your first cigarette?
   - After 60 minutes (0)
   - 31-60 minutes (1)
   - 6-30 minutes (2)
   - Within 5 minutes (3)

2. Do you find it difficult to refrain from smoking in places where it is forbidden?
   - No (0)
   - Yes (1)

3. Which cigarette would you hate most to give up?
   - The first in the morning (1)
   - Any other (0)

4. How many cigarettes per day do you smoke?
   - 10 or less (0)
   - 11-20 (1)
   - 21-30 (2)
   - 31 or more (3)

5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?
   - No (0)
   - Yes (1)

6. Do you smoke even if you are so ill that you are in bed most of the day?
   - No (0)
   - Yes (1)

* Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: A revision of the Fagerstrom Tolerance Questionnaire. British Journal of Addictions 1991;86:1119-27

Fagerstrom Test for Nicotine Dependence (cont.)

Your score was:_____

Your level of dependence on nicotine is:

0-2 Very low dependence	6-7 High dependence
3-4 Low dependence	8-10 Very high dependence
5 Medium dependence	

Scores under 5: "Your level of nicotine dependence is still low. You should act now before your level of dependence increases."

Score of 5: "Your level of nicotine dependence is moderate. If you don't quit soon, your level of dependence on nicotine will increase until you may be seriously addicted. Act now to end your dependence on nicotine."

Score over 7: "Your level of dependence is high. You aren't in control of your smoking – it is in control of you! When you make the decision to quit, you may want to talk with your doctor about nicotine replacement therapy or other medications to help you break your addiction."

Ujian Fagerstrom Untuk Ketagihan Nikotin

Adakah merokok "hanya satu tabiat" atau "adakah anda ketagih?" Sila jalani ujian ini untuk mengetahui tahap ketagihan nikotin anda.

1/ Bilakah anda menghisap rokok pertama anda selepas bangun dari tidur?

- Selepas 60 minit (0)
- 31 – 60 minit (1)
- 6-30 minit (2)
- Dalam masa 5 minit (3)

2/ Adakah anda berasa sukar untuk menahan diri dari merokok di kawasan larangan merokok?

- Tidak (0)
- Ya (1)

3/ Rokok yang mana satu paling sukar untuk berhenti ?

- Yang pertama pada waktu pagi (1)
- Yang lain (0)

4/ Berapa batang rokok yang anda hisap dalam sehari?

- 10 atau kurang (0)
- 11-20 (1)
- 21-30 (2)
- 31 atau lebih (3)

5/ Adakah anda merokok lebih kerap semasa beberapa jam pertama selepas bangun dari tidur berbanding pada waktu lain?

- Tidak (0)
- Ya (1)

6/ Adakah anda merokok meskipun ketika anda sakit dan terlantar di katil sepanjang hari?

- Tidak (0)
- Ya (1)

Tandakan markah

Markah anda:

0-2 ketagihan sangat rendah

3-4 ketagihan rendah

5 ketagihan sederhana

6-7 ketagihan tinggi

8-10 ketagihan sangat tinggi

Tahap ketagihan nikotin anda ialah:

Markah kurang daripada 5:

"Tahap ketagihan nikotin anda masih rendah. Anda perlu bertindak sekarang sebelum tahap ketagihan meningkat."

Markah ialah 5:

"Tahap ketagihan nikotin anda adalah sederhanda. Jika anda tidak berhenti segara, tahap ketagihan nikotin anda akan meningkat sehingga anda mungkin mengalami ketagihan yang serius. Bertindak sekarang untuk menghentikan ketagihan nikotin anda."

Markah lebih daripada 7:

" Tahap ketagihan anda adalah tinggi. Anda tidak dapat mengawal tabiat merokok anda- sebaliknya ia mengawal anda! Apabila anda membuat kepuusan untuk berhenti, mungkin anda mahu bertanya kepada doctor anda mengenai terapi penggantian nikotin atau ubat-ubatan lain untuk membantu anda mengatasi ketagihan anda."